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CH/CHEM. ENG. (STIC)

Scientific and Technical Information Center

SEARCH REQUEST FORM

ACCESS DB # 167819

PLEASE PRINT CLEARLY

169604

2nd time: 168877

Requester's Full Name: PATRICIA LEITH Examiner #: 77489 Date: 10/05/05

Art Unit: 1655 Phone Number: 2-0968 Serial Number: 091736,051

Location (Bldg/Room#): 3D21 (Mailbox #): 3C18 Results Format Preferred (circle): PAPER DISK

To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following:

Title of Invention:

Inventors (please provide full names): Ke, Hua Zhu ; Thompson, DAVID O.

Earliest Priority Date: 2/28/1996

Search Topic:

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known.

\*For Sequence Searches Only\* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

- Please search compounds of claim 3 (any) with compounds of claim 4 (all combinations).

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Please also search combinations with from above  
osteoporosis + bone loss.

- Please search the compounds of claim 3 and osteoporosis + bone loss

For 103  
Rejection

- Please search the compounds of claim 4 and osteoporosis + bone loss (may search Paggi, osteo?, bone?)

STAFF USE ONLY

Searcher: \_\_\_\_\_

Searcher Phone #: \_\_\_\_\_

Searcher Location: \_\_\_\_\_

Date Searcher Picked Up: \_\_\_\_\_

Date Completed: 10-14-5

Searcher Prep & Review Time: \_\_\_\_\_

Online Time: \_\_\_\_\_

Type of Search

\_\_\_\_ NA Sequence (#)

\_\_\_\_ AA Sequence (#)

\_\_\_\_ Structure (#)

\_\_\_\_ Bibliographic

\_\_\_\_ Litigation

\_\_\_\_ Fulltext

\_\_\_\_ Other

Vendors and cost where applicable

\_\_\_\_ STN \_\_\_\_\_ Dialog

\_\_\_\_ Questel/Orbit \_\_\_\_\_ Lexis/Nexis

\_\_\_\_ Westlaw \_\_\_\_\_ WWW/Internet

\_\_\_\_ In-house sequence systems

\_\_\_\_ Commercial \_\_\_\_\_ Oligomer \_\_\_\_\_ Score/Length  
\_\_\_\_ Interference \_\_\_\_\_ SPDI \_\_\_\_\_ Encode/Transl  
\_\_\_\_ Other (specify)

=> d 1-4

L26 ANSWER 1 OF 4 REGISTRY COPYRIGHT 2005 ACS on STN

RN 84449-90-1 REGISTRY

ED Entered STN: 16 Nov 1984

CN Methanone, [6-hydroxy-2-(4-hydroxyphenyl)benzo[b]thien-3-yl][4-[2-(1-piperidinyl)ethoxy]phenyl]- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN Keoxifene

CN LY 139481

CN Raloxifene

CN [2-(4-Hydroxyphenyl)-6-hydroxybenzo[b]thien-3-yl][4-(2-(1-piperidinyl)ethoxy)phenyl]methanone

FS 3D CONCORD

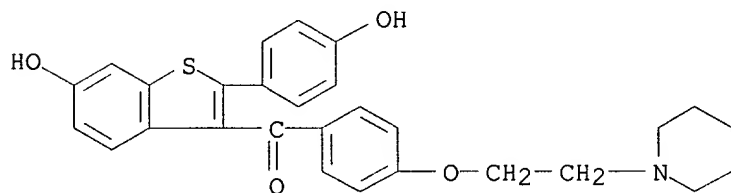
MF C28 H27 N O4 S

CI COM

LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN\*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CIN, CSCHEM, DDFU, DIOGENES, DRUGU, EMBASE, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK\*, PATDPASPC, PHAR, PROMT, PROUDDR, RTECS\*, SCISEARCH, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL

(\*File contains numerically searchable property data)

Other Sources: WHO



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1288 REFERENCES IN FILE CA (1907 TO DATE)

29 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

1295 REFERENCES IN FILE CAPLUS (1907 TO DATE)

ED Entered STN: 16 Nov 1984

L26 ANSWER 2 OF 4 REGISTRY COPYRIGHT 2005 ACS on STN

RN 82413-20-5 REGISTRY

ED Entered STN: 16 Nov 1984

CN Phenol, 3-[(1E)-1-[4-[2-(dimethylamino)ethoxy]phenyl]-2-phenyl-1-butenyl]- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Phenol, 3-[1-[4-[2-(dimethylamino)ethoxy]phenyl]-2-phenyl-1-butenyl]-, (E)-

OTHER NAMES:

CN 3-Hydroxytamoxifen

CN Droloxifene

CN E-Droloxifene

CN K 060

CN K 060E

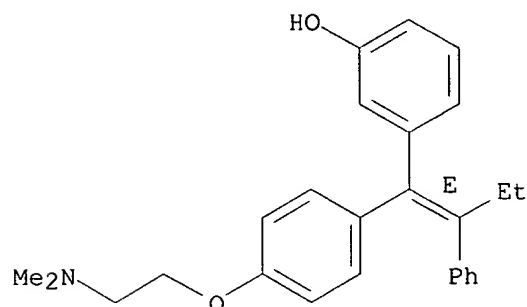
CN K 21.060E

FS STEREOSEARCH

MF C26 H29 N O2

CI COM  
 LC STN Files: ADISINSIGHT, ADISNEWS, BEILSTEIN\*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CHEMLIST, CIN, CSCHEM, DDFU, DRUGU, EMBASE, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK\*, PHAR, PROMT, PROUSDDR, RTECS\*, SYNTHLINE, TOXCENTER, ULIDAT, USAN, USPAT2, USPATFULL  
 (\*File contains numerically searchable property data)  
 Other Sources: WHO

Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

291 REFERENCES IN FILE CA (1907 TO DATE)  
 3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
 292 REFERENCES IN FILE CAPLUS (1907 TO DATE)

ED Entered STN: 16 Nov 1984

L26 ANSWER 3 OF 4 REGISTRY COPYRIGHT 2005 ACS on STN

RN **68047-06-3** REGISTRY

ED Entered STN: 16 Nov 1984

CN Phenol, 4-[(1Z)-1-[4-[2-(dimethylamino)ethoxy]phenyl]-2-phenyl-1-butenyl]-  
 (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Phenol, 4-[1-[4-[2-(dimethylamino)ethoxy]phenyl]-2-phenyl-1-butenyl]-,  
 (Z)-

OTHER NAMES:

CN (Z)-4-Hydroxytamoxifen

CN 4-Hydroxytamoxifen

CN 4-[(1Z)-1-[4-[2-(dimethylamino)ethoxy]phenyl]-2-phenyl-1-butenyl]phenol

CN Hydroxytamoxifen

CN ICI 79280

CN trans-4-Hydroxytamoxifen

CN trans-Hydroxytamoxifen

FS STEREOSEARCH

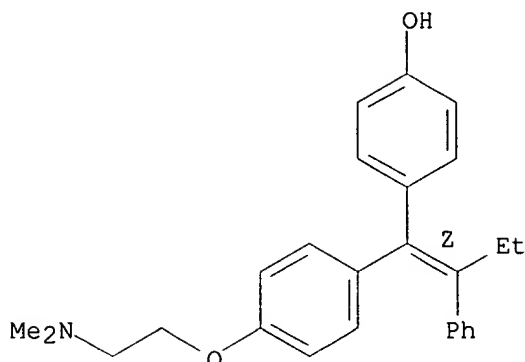
DR 65213-48-1, 72732-26-4, 76276-99-8

MF C26 H29 N O2

CI COM

LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN\*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CEN, CHEMCATS, CIN, CSCHEM, DDFU, DRUGU, EMBASE, IMSDRUGNEWS, IPA, NIOSHTIC, PHAR, PROMT, RTECS\*, TOXCENTER, USPAT2, USPATFULL  
 (\*File contains numerically searchable property data)

Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1285 REFERENCES IN FILE CA (1907 TO DATE)

35 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

1291 REFERENCES IN FILE CAPLUS (1907 TO DATE)

ED Entered STN: 16 Nov 1984

L26 ANSWER 4 OF 4 REGISTRY COPYRIGHT 2005 ACS on STN

RN 10540-29-1 REGISTRY

ED Entered STN: 16 Nov 1984

CN Ethanamine, 2-[4-[(1Z)-1,2-diphenyl-1-butenyl]phenoxy]-N,N-dimethyl- (9CI)  
(CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Ethanamine, 2-[4-(1,2-diphenyl-1-butenyl)phenoxy]-N,N-dimethyl-, (Z)-

CN Ethylamine, 2-[p-(1,2-diphenyl-1-butenyl)phenoxy]-N,N-dimethyl-, (Z)-  
(8CI)

OTHER NAMES:

CN ICI 47699

CN Mammaton

CN Tamoxifen

CN trans-Tamoxifen

CN Z-Tamoxifen

FS STEREOSEARCH

MF C26 H29 N O

CI COM

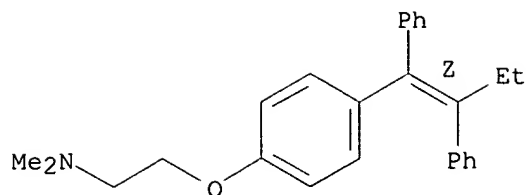
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN\*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DIOGENES, DRUGU, EMBASE, HSDB\*, IMSCOSEARCH, IMSPATENTS, IPA, MEDLINE, MRCK\*, MSDS-OHS, NIOSHTIC, PHAR, PROMT, PS, RTECS\*, SCISEARCH, SPECINFO, TOXCENTER, ULIDAT, USAN, USPAT2, USPATFULL, VETU

(\*File contains numerically searchable property data)

Other Sources: EINECS\*\*, WHO

(\*\*Enter CHEMLIST File for up-to-date regulatory information)

Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

6467 REFERENCES IN FILE CA (1907 TO DATE)

154 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

6488 REFERENCES IN FILE CAPLUS (1907 TO DATE)

ED Entered STN: 16 Nov 1984

=> => d 1-7

L27 ANSWER 1 OF 7 REGISTRY COPYRIGHT 2005 ACS on STN

RN 193274-89-4 REGISTRY

ED Entered STN: 29 Aug 1997

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[6-[2-(1-pyrrolidinyl)ethoxy]-3-pyridinyl]-, (5R,6R)-rel- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[6-[2-(1-pyrrolidinyl)ethoxy]-3-pyridinyl]-, cis-

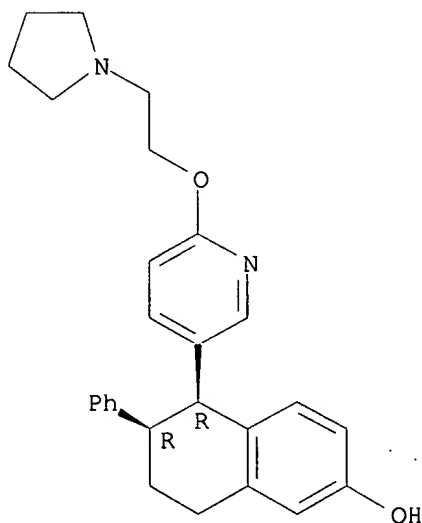
FS STEREOSEARCH

MF C27 H30 N2 O2

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL

Relative stereochemistry.



## \*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

19 REFERENCES IN FILE CA (1907 TO DATE)  
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
19 REFERENCES IN FILE CAPLUS (1907 TO DATE)

ED Entered STN: 29 Aug 1997

L27 ANSWER 2 OF 7 REGISTRY COPYRIGHT 2005 ACS on STN

RN 180916-16-9 REGISTRY

ED Entered STN: 18 Sep 1996

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R-cis)-

OTHER NAMES:

CN Lasofoxifene

FS STEREOSEARCH

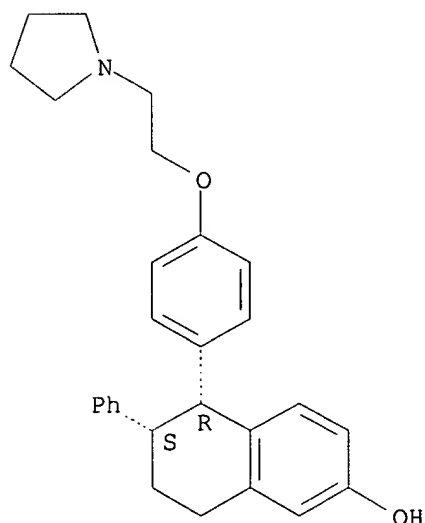
MF C28 H31 N O2

CI COM

SR CA

LC STN Files: ADISINSIGHT, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, DDFU, DRUGU, EMBASE, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, PROUSDDR, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL

Absolute stereochemistry. Rotation (-).



## \*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

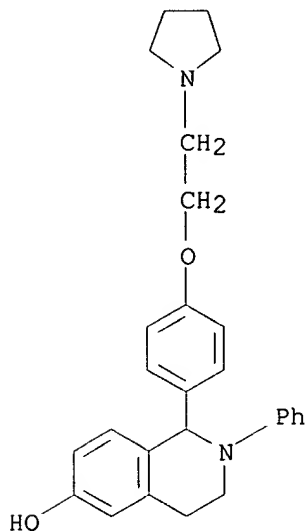
96 REFERENCES IN FILE CA (1907 TO DATE)  
6 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
96 REFERENCES IN FILE CAPLUS (1907 TO DATE)

ED Entered STN: 18 Sep 1996

L27 ANSWER 3 OF 7 REGISTRY COPYRIGHT 2005 ACS on STN

RN 180916-15-8 REGISTRY

ED Entered STN: 18 Sep 1996  
CN 6-Isoquinolinol, 1,2,3,4-tetrahydro-2-phenyl-1-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C27 H30 N2 O2  
CI COM  
SR CA  
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPAT2, USPATFULL

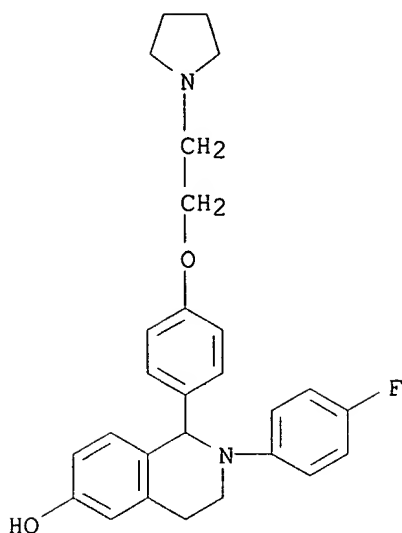


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

22 REFERENCES IN FILE CA (1907 TO DATE)  
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
22 REFERENCES IN FILE CAPLUS (1907 TO DATE)

ED Entered STN: 18 Sep 1996

L27 ANSWER 4 OF 7 REGISTRY COPYRIGHT 2005 ACS on STN  
RN **180916-14-7** REGISTRY  
ED Entered STN: 18 Sep 1996  
CN 6-Isoquinolinol, 2-(4-fluorophenyl)-1,2,3,4-tetrahydro-1-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C27 H29 F N2 O2  
CI COM  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

21 REFERENCES IN FILE CA (1907 TO DATE)  
 1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
 21 REFERENCES IN FILE CAPLUS (1907 TO DATE)

ED Entered STN: 18 Sep 1996

L27 ANSWER 5 OF 7 REGISTRY COPYRIGHT 2005 ACS on STN

RN **180915-86-0** REGISTRY

ED Entered STN: 18 Sep 1996

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-(4-hydroxyphenyl)-5-[4-[2-(1-piperidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-(4-hydroxyphenyl)-5-[4-[2-(1-piperidinyl)ethoxy]phenyl]-, cis-

FS STEREOSEARCH

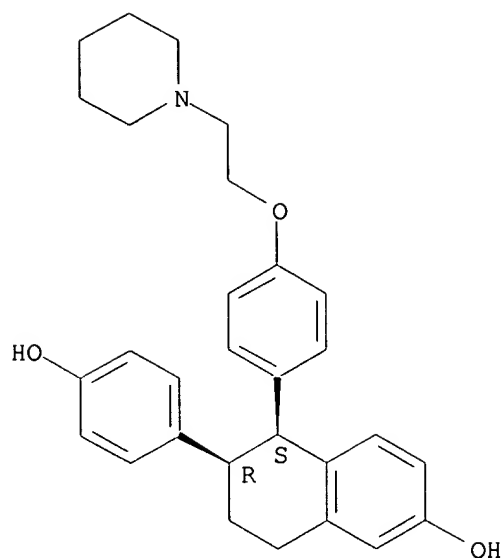
MF C29 H33 N O3

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL

Relative stereochemistry.





\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

20 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

20 REFERENCES IN FILE CAPLUS (1907 TO DATE)

ED Entered STN: 18 Sep 1996

L27 ANSWER 6 OF 7 REGISTRY COPYRIGHT 2005 ACS on STN

RN **180915-84-8** REGISTRY

ED Entered STN: 18 Sep 1996

CN 2-Naphthalenol, 6-(4-fluorophenyl)-5,6,7,8-tetrahydro-5-[4-[2-(1-piperidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 2-Naphthalenol, 6-(4-fluorophenyl)-5,6,7,8-tetrahydro-5-[4-[2-(1-piperidinyl)ethoxy]phenyl]-, cis-

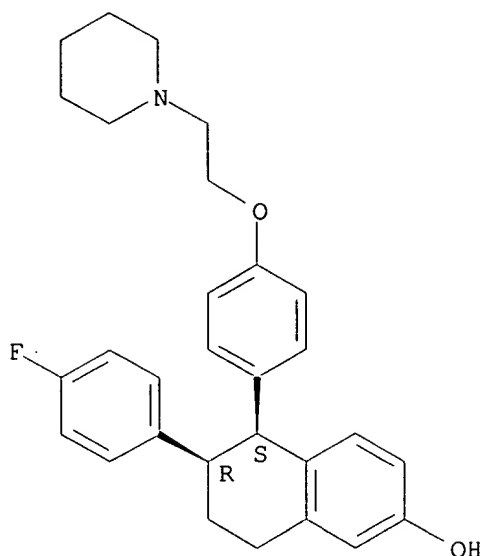
FS STEREOSEARCH

MF C29 H32 F N O2

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL

Relative stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

21 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

21 REFERENCES IN FILE CAPLUS (1907 TO DATE)

ED Entered STN: 18 Sep 1996

L27 ANSWER 7 OF 7 REGISTRY COPYRIGHT 2005 ACS on STN

RN **180915-78-0** REGISTRY

ED Entered STN: 18 Sep 1996

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, cis-

OTHER NAMES:

CN CP 319609

FS STEREOSEARCH

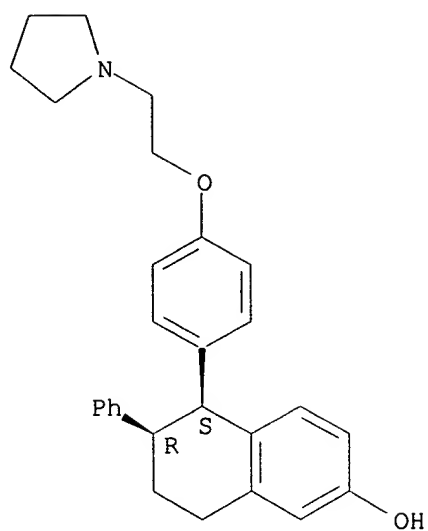
MF C28 H31 N O2

CI COM

SR CA

LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPAT2, USPATFULL

Relative stereochemistry.



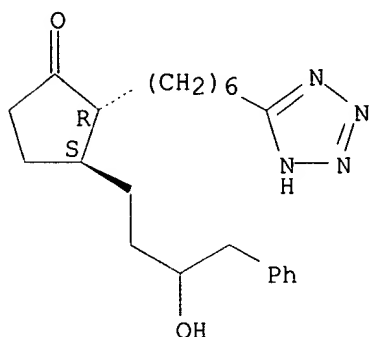
28 REFERENCES IN FILE CA (1907 TO DATE)  
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
28 REFERENCES IN FILE CAPLUS (1907 TO DATE)

ED Entered STN: 18 Sep 1996

=&gt; d 1-6

L37 ANSWER 1 OF 6 REGISTRY COPYRIGHT 2005 ACS on STN  
 RN 195962-24-4 REGISTRY  
 ED Entered STN: 24 Oct 1997  
 CN Cyclopentanone, 3-(3-hydroxy-4-phenylbutyl)-2-[6-(1H-tetrazol-5-yl)hexyl]-  
 , (2R,3S)- (9CI) (CA INDEX NAME)  
 OTHER CA INDEX NAMES:  
 CN Cyclopentanone, 3-(3-hydroxy-4-phenylbutyl)-2-[6-(1H-tetrazol-5-yl)hexyl]-  
 , [2R-(2 $\alpha$ ,3 $\beta$ )]-[partial]-  
 FS STEREOSEARCH  
 MF C22 H32 N4 O2  
 SR CA  
 LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.

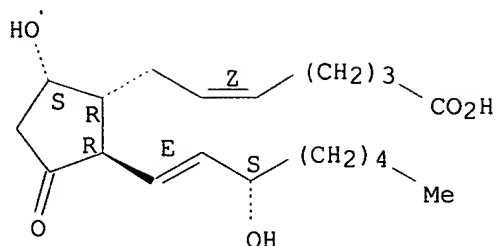


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

2 REFERENCES IN FILE CA (1907 TO DATE)  
 2 REFERENCES IN FILE CAPLUS (1907 TO DATE)  
 ED Entered STN: 24 Oct 1997

L37 ANSWER 2 OF 6 REGISTRY COPYRIGHT 2005 ACS on STN  
 RN 41598-07-6 REGISTRY  
 ED Entered STN: 16 Nov 1984  
 CN Prosta-5,13-dien-1-oic acid, 9,15-dihydroxy-11-oxo-, (5Z,9 $\alpha$ ,13E,15S)-  
 (9CI) (CA INDEX NAME)  
 OTHER NAMES:  
 CN 11-Dehydroprostaglandin F2 $\alpha$   
 CN PGD2  
 CN Prostaglandin D2  
 FS STEREOSEARCH  
 MF C20 H32 O5  
 CI COM  
 LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN\*, BIOBUSINESS, BIOSIS,  
 BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CHEMCATS, CIN, CSCHEM, DDFU,  
 DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MSDS-OHS,  
 NAPRALERT, PROMT, PROUSDDR, RTECS\*, SYNTHLINE, TOXCENTER, USPAT2,  
 USPATFULL  
 (\*File contains numerically searchable property data)

Absolute stereochemistry.  
 Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

3196 REFERENCES IN FILE CA (1907 TO DATE)

40 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

3199 REFERENCES IN FILE CAPLUS (1907 TO DATE)

ED Entered STN: 16 Nov 1984

L37 ANSWER 3 OF 6 REGISTRY COPYRIGHT 2005 ACS on STN

RN 17968-82-0 REGISTRY

ED Entered STN: 16 Nov 1984

CN Prost-13-en-1-oic acid, 9,15-dihydroxy-11-oxo-, (9 $\alpha$ ,13E,15S)- (9CI)  
(CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Cyclopentaneheptanoic acid, 5-hydroxy-2-(3-hydroxy-1-octenyl)-3-oxo- (7CI, 8CI)

OTHER NAMES:

CN 2-Hydroxy-5-(3S-hydroxy-1-octenyl)-3-oxocyclopentaneheptanoic acid

CN 9 $\alpha$ ,15-Dihydroxy-11-ketoprost-13-enoic acid

CN **PGD1**

CN Prostaglandin D1

CN Prostaglandin Fl $\alpha$ , 11-dehydro-

FS STEREOSEARCH

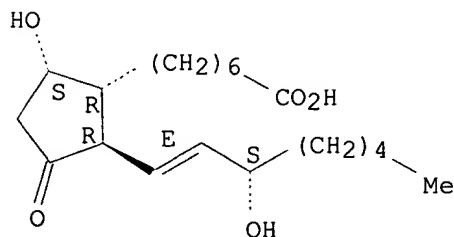
DR 5598-36-7

MF C20 H34 O5

LC STN Files: AGRICOLA, BEILSTEIN\*, BIOSIS, CA, CAOLD, CAPLUS, CASREACT, CHEMCATS, CSCHEM, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, RTECS\*, TOXCENTER, USPAT2, USPATFULL  
(\*File contains numerically searchable property data)

Absolute stereochemistry.

Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

72 REFERENCES IN FILE CA (1907 TO DATE)  
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
72 REFERENCES IN FILE CAPLUS (1907 TO DATE)  
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

ED Entered STN: 16 Nov 1984

L37 ANSWER 4 OF 6 REGISTRY COPYRIGHT 2005 ACS on STN

RN 745-65-3 REGISTRY

ED Entered STN: 16 Nov 1984

CN Prost-13-en-1-oic acid, 11,15-dihydroxy-9-oxo-, (11 $\alpha$ ,13E,15S)- (9CI)  
(CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Cyclopentaneheptanoic acid, 3-hydroxy-2-(3-hydroxy-1-octenyl)-5-oxo-, (-)-  
(8CI)

CN Cyclopentaneheptanoic acid, 3 $\alpha$ -hydroxy-2-(3-hydroxy-1-octenyl)-5-oxo-  
(7CI)

OTHER NAMES:

CN (-)-Prostaglandin E1

CN 11 $\alpha$ ,15(S)-Dihydroxy-9-oxo-13-trans-prostenoic acid

CN 11 $\alpha$ ,15 $\alpha$ -Dihydroxy-9-oxo-13-trans-prostenoic acid

CN Alprostadil

CN Alprox TD

CN Caveject

CN Caverject

CN 1-PGE1

CN 1-Prostaglandin E1

CN Liple

CN Lipoprost

CN Liprostin

CN Minprog

CN NSC 165559

CN ONO 1608

CN Palux

CN **PGE1**

CN Prostaglandin E1

CN Prostandin

CN Prostandin 500

CN Prostlin VR Pediatric

CN Prostivas

CN SEPA-alprostadil

CN SEPA-PGE1

CN SEPA-prostaglandin E1

CN Topiglan

CN U 10136

CN Vasaprostan

FS STEREOSEARCH

DR 50-83-9, 22299-37-2, 50865-30-0

MF C20 H34 O5

CI COM

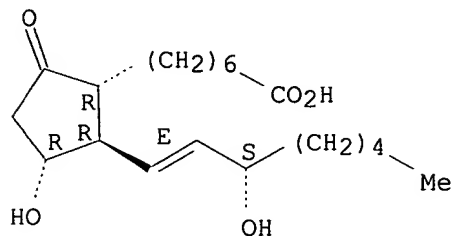
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN\*,  
BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT,  
CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGU,  
EMBASE, IFICDB, IFIPAT, IFIUDB, IMSCSEARCH, IMSDRUGNEWS, IMSPATENTS,  
IMSRESEARCH, IPA, MEDLINE, MRCK\*, MSDS-OHS, NAPRALERT, NIOSHTIC, PHAR,  
PROMT, PROUSDDR, RTECS\*, SCISEARCH, SPECINFO, TOXCENTER, USAN, USPAT2,  
USPATFULL, VETU

(\*File contains numerically searchable property data)

Other Sources: EINECS\*\*, WHO

(\*\*Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.  
Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

8853 REFERENCES IN FILE CA (1907 TO DATE)  
157 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
8855 REFERENCES IN FILE CAPLUS (1907 TO DATE)  
2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

ED Entered STN: 16 Nov 1984

L37 ANSWER 5 OF 6 REGISTRY COPYRIGHT 2005 ACS on STN

RN 551-11-1 REGISTRY

ED Entered STN: 16 Nov 1984

CN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-,  
(5Z,9α,11α,13E,15S)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 5-Heptenoic acid, 7-[3,5-dihydroxy-2-(3-hydroxy-1-octenyl)cyclopentyl]-  
(8CI)

OTHER NAMES:

CN (+)-Prostaglandin F2α

CN 7-[3,5-Dihydroxy-2-(3-hydroxy-1-octenyl)cyclopentyl]-5-heptenoic acid

CN 9α,11α,15(S)-Trihydroxy-5-cis-13-trans-prostadienoic acid

CN 9α,11α-PGF2

CN 9α,11α-PGF2α

CN Amoglandin

CN Cyclosin

CN Cyclosin (pharmaceutical)

CN Dinifertin

CN Dinoprost

CN Enzaprost

CN Enzaprost F

CN Glandin N

CN Panacelan

CN **PGF2α**

CN Prostaglandin F2

CN Prostaglandin F2α

CN Prostarmon F

CN Prostin F 2 alpha

CN Protamodin

CN U 14583

FS STEREOSEARCH

DR 13535-33-6, 99437-94-2

MF C20 H34 O5

CI COM

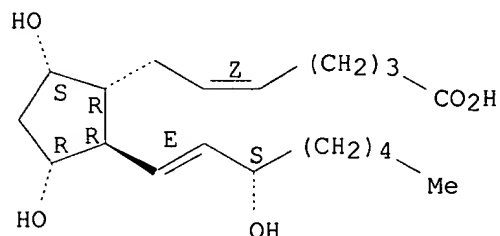
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN\*, BIOBUSINESS,  
BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB,  
CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DRUGU, EMBASE, HSDB\*, IFICDB,

IFIPAT, IFIUDB, IPA, MEDLINE, MRCK\*, NAPRALERT, NIOSHTIC, PHAR, PROMT,  
PS, RTECS\*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL, VETU

(\*File contains numerically searchable property data)

Other Sources: WHO

Absolute stereochemistry.  
Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

13769 REFERENCES IN FILE CA (1907 TO DATE)

162 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

13773 REFERENCES IN FILE CAPLUS (1907 TO DATE)

2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

ED Entered STN: 16 Nov 1984

L37 ANSWER 6 OF 6 REGISTRY COPYRIGHT 2005 ACS on STN

RN 363-24-6 REGISTRY

ED Entered STN: 16 Nov 1984

CN Prosta-5,13-dien-1-oic acid, 11,15-dihydroxy-9-oxo-,  
(5Z,11α,13E,15S)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 5-Heptenoic acid, 7-[3-hydroxy-2-(3-hydroxy-1-octenyl)-5-oxocyclopentyl]-  
(8CI)

CN 5-Heptenoic acid, 7-[3α-hydroxy-2-(3-hydroxy-1-octenyl)-5-  
oxocyclopentyl]- (7CI)

OTHER NAMES:

CN (-)-Prostaglandin E2

CN (15S)-Prostaglandin E2

CN 11α,15α-Dihydroxy-9-ketoprost-5,13-dienoic acid

CN 11α,15α-Dihydroxy-9-oxo-5-cis,13-trans-prostadienoic acid

CN Cervidil

CN Cerviprime

CN Cerviprost

CN Dinoprostone

CN Enzaprost E

CN Glandin

CN 1-PGE2

CN 1-Prostaglandin E2

CN Minprostin E2

CN Minprostin E2

CN NSC 165560

CN NSC 196514

CN **PGE2**

CN Prepidil

CN Primiprost

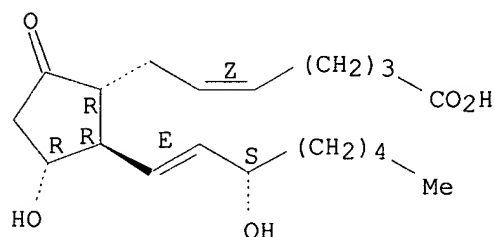
CN Propess

CN Prostaglandin E2



CN Prostamon E  
 CN Prostenon  
 CN Prostenone  
 CN Prostlin  
 CN Prostlin (prostaglandin)  
 CN Prostlin E2  
 CN U 12062  
 FS STEREOSEARCH  
 MF C20 H32 O5  
 CI COM  
 LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN\*, BIOBUSINESS, BIOSIS,  
 BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS,  
 CHEMLIST, CIN, CSCHM, CSNB, DDFU, DIOGENES, DRUGU, EMBASE, IFICDB,  
 IFIPAT, IFIUDB, IMSCSEARCH, IPA, MEDLINE, MRCK\*, MSDS-OHS, NAPRALERT,  
 NIOSHTIC, PHAR, PROMT, PS, RTECS\*, SPECINFO, TOXCENTER, USAN, USPAT2,  
 USPATFULL, VETU  
 (\*File contains numerically searchable property data)  
 Other Sources: EINECS\*\*, WHO  
 (\*\*Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.  
 Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

25922 REFERENCES IN FILE CA (1907 TO DATE)  
 126 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
 25954 REFERENCES IN FILE CAPLUS (1907 TO DATE)  
 1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

ED Entered STN: 16 Nov 1984

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L26      4 SEA FILE=REGISTRY ABB=ON (82413-20-5 OR 84449-90-1 OR
10540-29-1 OR 68047-06-3)/RN
L27      7 SEA FILE=REGISTRY ABB=ON (180915-84-8 OR 180915-78-0 OR
180916-16-9 OR 193274-89-4 OR 180916-14-7 OR 180915-86-0 OR
180916-15-8)/RN
L28      11 SEA FILE=REGISTRY ABB=ON L26 OR L27
L29      4 SEA FILE=REGISTRY ABB=ON (PGD1 OR PGD2 OR PGE2 OR PGE1 OR
PGF2 OR PGF2A)/CN
L30      1 SEA FILE=REGISTRY ABB=ON PGF2A/CN
L31      5 SEA FILE=REGISTRY ABB=ON L29 OR L30
L32      6 SEA FILE=REGISTRY ABB=ON L31 OR 195962-24-4/RN
L33      10983 SEA FILE=HCAPLUS ABB=ON L28 OR ?DROLOXIFENE? OR ?RALOXIFENE?
OR ?TAMOXIFEN?
L34      73 SEA FILE=HCAPLUS ABB=ON L33 AND (L32 OR PGD1 OR PGD2 OR PGE2
OR PGE1 OR PGF2 OR PGF2A OR PGF2A)
L35      6 SEA FILE=HCAPLUS ABB=ON L34 AND (?BONE?(W) (?LOSS? OR ?LOSE?
OR ?RESORP) OR ?OSTEOPOROS? OR ?PAGET?)
L37      21 SEA L35
L38      16 DUP REMOV L37 (5 DUPLICATES REMOVED)
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L38 ANSWER 1 OF 16 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights
reserved on STN
ACCESSION NUMBER: 2005196000 EMBASE
TITLE: Re: Continuing outcomes relevant to evista: Breast cancer
incidence in postmenopausal osteoporotic women in a
randomized trial of raloxifene (multiple letters)
[2].
AUTHOR: Yalcin B.; Buyukcelik A.; Yalcin S.; Utkan G.; Doruk H.;
Dogan M.; Altan M.; Martino S.; Cauley J.A.; Barrett-Connor
E.; Powles T.J.; Mershon J.; Disch D.; Secrest R.J.;
Cummings S.R.
CORPORATE SOURCE: Dr. B. Yalcin, Department of Medical Oncology, Ankara
University School of Medicine, TR-06100 Sıhhiye, Ankara,
Turkey. bulyalcin@yahoo.com
SOURCE: Journal of the National Cancer Institute, (6 Apr 2005) Vol.
97, No. 7, pp. 542-543.
ISSN: 0027-8874 CODEN: JNCIAM
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Letter
FILE SEGMENT: 010 Obstetrics and Gynecology
016 Cancer
030 Pharmacology
033 Orthopedic Surgery
037 Drug Literature Index
LANGUAGE: English
ENTRY DATE: Entered STN: 20050519
Last Updated on STN: 20050519
DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER
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L38 ANSWER 2 OF 16 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2004642870 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15619569
TITLE: Stimulative effects of Drynariae Rhizoma extracts on the
proliferation and differentiation of osteoblastic MC3T3-E1
cells.
AUTHOR: Jeong Ji-Cheon; Lee Jae-Wook; Yoon Cheol-Ho; Lee
Young-Choon; Chung Kang-Hyun; Kim Min-Gon; Kim Cheorl-Ho
```

CORPORATE SOURCE: Department of Internal Medicine, Biochemistry and Molecular Biology, College of Oriental Medicine, Dongguk University and National Research Laboratory for Glycobiology, Kyungju 780-714, Korea.

SOURCE: Journal of ethnopharmacology, (2005 Jan 15) 96 (3) 489-95.  
Electronic Publication: 2004-11-14.  
Journal code: 7903310. ISSN: 0378-8741.

PUB. COUNTRY: Ireland

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200505

ENTRY DATE: Entered STN: 20041228  
Last Updated on STN: 20050525  
Entered Medline: 20050524

AB Pharmacological factors are needed to prevent **bone loss** that occurs with increasing age. The chemical compounds that act on bone metabolism in herbal medicines, however, are poorly understood. Effects of traditional Korean medicine, *Drynariae Rhizoma* [*Drynaria fortunei* (kunze) J. Sm] extract (DR), on the osteoblastic proliferation and differentiation were investigated. The effect of DR, a natural phyto herb, on the proliferation and osteoblastic differentiation in non-transformed osteoblastic cells (MC3T3-E1) was studied. DR dose-dependently increased DNA synthesis (significant at 50-150 microg/ml). DR increased alkaline phosphatase (ALP) activity and prolyl hydroxylase activity of MC3T3-E1 cells (50-150 microg/ml). Antiestrogen **tamoxifen** eleminated the stimulation of proliferation and ALP activity of MC3T3-E1, which were induced by DR. DR at concentrations ranged from 30-100 microg/ml inhibited prostaglandin E2 production in MC3T3-E1. These results indicate that DR directly stimulates cell proliferation and differentiation of osteoblasts. These results also suggest and DR is effective for bone anti-resorptive action in bone cells.

L38 ANSWER 3 OF 16 MEDLINE on STN DUPLICATE 2

ACCESSION NUMBER: 2005341133 MEDLINE

DOCUMENT NUMBER: PubMed ID: 15922308

TITLE: The licorice root derived isoflavan glabridin increases the function of osteoblastic MC3T3-E1 cells.

AUTHOR: Choi Eun-Mi

CORPORATE SOURCE: Department of Food and Nutrition, Kyung Hee University, 1, Hoegi-dong, Dongdaemun-gu, Seoul 130-701, Republic of Korea.. cheunmi@hanmail.net

SOURCE: Biochemical pharmacology, (2005 Aug 1) 70 (3) 363-8.  
Journal code: 0101032. ISSN: 0006-2952.

PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200508

ENTRY DATE: Entered STN: 20050706  
Last Updated on STN: 20050819  
Entered Medline: 20050818

AB Glabridin, an isoflavan purified from licorice root, exhibits diverse biological activities, including estrogen-like activity. To investigate the bioactivities of glabridin, which act on bone metabolism, the effects of glabridin on the function of mouse osteoblastic cell line (MC3T3-E1) and the production of local factors in osteoblasts were studied. Glabridin (1-10microM) significantly increased the growth of MC3T3-E1 cells and caused a significant elevation of alkaline phosphatase (ALP) activity, collagen content and osteocalcin secretion in the cells

( $P < 0.05$ ). The effect of glabridin (10  $\mu$ M) in increasing ALP activity and collagen content was completely prevented by the presence of 10(-6)M cycloheximide and 10(-6)M **tamoxifen**, suggesting that glabridin's effect results from a newly synthesized protein component and might be partly involved in estrogen action. Then, the effects of glabridin on the TNF-alpha-induced apoptosis and production of prostaglandin E2 (**PGE2**) and nitric oxide (NO) in osteoblasts were examined. Treatment with glabridin (1-10  $\mu$ M) prevented apoptosis induced by TNF-alpha (10(-10)M) in osteoblastic cells. Moreover, glabridin (50  $\mu$ M) decreased the 10(-10)M TNF-alpha-induced production of **PGE2** and NO in osteoblasts. Our data indicate that the enhancement of osteoblast function by glabridin may result in the prevention for **osteoporosis** and inflammatory bone diseases.

L38 ANSWER 4 OF 16 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2005222945 EMBASE  
 TITLE: Aromatase inhibitors in the treatment of breast cancer.  
 AUTHOR: Brueggemeier R.W.; Hackett J.C.; Diaz-Cruz E.S.  
 CORPORATE SOURCE: Dr. R.W. Brueggemeier, College of Pharmacy, Ohio State University, 500 West 12th Avenue, Columbus, OH 43210-1291, United States. Brueggemeier.1@osu.edu  
 SOURCE: Endocrine Reviews, (2005) Vol. 26, No. 3, pp. 331-345.  
 Refs: 166  
 ISSN: 0163-769X CODEN: ERVIDP  
 COUNTRY: United States  
 DOCUMENT TYPE: Journal; General Review  
 FILE SEGMENT: 003 Endocrinology  
 010 Obstetrics and Gynecology  
 016 Cancer  
 037 Drug Literature Index  
 038 Adverse Reactions Titles  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 ENTRY DATE: Entered STN: 20050616  
 Last Updated on STN: 20050616

AB Estradiol, the most potent endogenous estrogen, is biosynthesized from androgens by the cytochrome P450 enzyme complex called aromatase. Aromatase is present in breast tissue, and intratumoral aromatase is the source of local estrogen production in breast cancer tissues. Inhibition of aromatase is an important approach for reducing growth-stimulatory effects of estrogens in estrogen-dependent breast cancer. Steroidal inhibitors that have been developed to date build upon the basic androstenedione nucleus and incorporate chemical substituents at varying positions on the steroid. Nonsteroidal aromatase inhibitors can be divided into three classes: aminoglutethimide-like molecules, imidazole/triazole derivatives, and flavonoid analogs. Mechanism-based aromatase inhibitors are steroidal inhibitors that mimic the substrate, are converted by the enzyme to a reactive intermediate, and result in the inactivation of aromatase. Both steroidal and non-steroidal aromatase inhibitors have shown clinical efficacy in the treatment of breast cancer. The potent and selective third-generation aromatase inhibitors, anastrozole, letrozole, and exemestane, were introduced into the market as endocrine therapy in postmenopausal patients failing antiestrogen therapy alone or multiple hormonal therapies. These agents are currently approved as first-line therapy for the treatment of postmenopausal women with metastatic estrogen-dependent breast cancer. Several clinical studies of aromatase inhibitors are currently focusing on the use of these agents in the adjuvant setting for the treatment of early breast cancer. Use of an aromatase inhibitor as initial therapy or after treatment with

**tamoxifen** is now recommended as adjuvant hormonal therapy for a postmenopausal woman with hormone-dependent breast cancer. Copyright .COPYRGT. 2005 by The Endocrine Society.

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ACCESSION NUMBER: 2004461452 EMBASE  
TITLE: Patent news.  
AUTHOR: Steele P.; Sparrowhawk M.  
CORPORATE SOURCE: P. Steele, Thomson Scientific, Middlesex House, 34-42  
Cleveland St., London W1T 4JE, United Kingdom.  
peter.steele@current-patents.com  
SOURCE: IDrugs, (2004) Vol. 7, No. 10, pp. 940-942.  
ISSN: 1369-7056 CODEN: IDRUFN  
COUNTRY: United Kingdom  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 006 Internal Medicine  
016 Cancer  
017 Public Health, Social Medicine and Epidemiology  
037 Drug Literature Index  
039 Pharmacy  
LANGUAGE: English  
ENTRY DATE: Entered STN: 20041112  
Last Updated on STN: 20041112

DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L38 ANSWER 6 OF 16 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2004438027 EMBASE  
TITLE: Complications of androgen deprivation therapy in men with  
prostate cancer.  
AUTHOR: Chen A.C.; Petrylak D.P.  
CORPORATE SOURCE: Dr. A.C. Chen, Department of Medicine, College of  
Physicians and Surgeons, Columbia University, 177 Fort  
Washington Avenue, New York, NY 10032, United States.  
acc23@columbia.edu  
SOURCE: Current Oncology Reports, (2004) Vol. 6, No. 3, pp.  
209-215.  
Refs: 59  
ISSN: 1523-3790 CODEN: CORUAT  
COUNTRY: United Kingdom  
DOCUMENT TYPE: Journal; General Review  
FILE SEGMENT: 016 Cancer  
028 Urology and Nephrology  
037 Drug Literature Index  
038 Adverse Reactions Titles  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ENTRY DATE: Entered STN: 20041028  
Last Updated on STN: 20041028

AB Androgen deprivation therapy (ADT) is indicated for the treatment of metastatic prostate cancer and locally advanced disease. In addition to sexual side effects, long-term ADT results in several other changes, including hot flashes; gynecomastia; changes in body composition, metabolism, and the cardiovascular system; **osteoporosis**; anemia; psychiatric and cognitive problems; and fatigue and diminished quality of life. This review discusses these complications of ADT and treatments aimed at reducing them. It is important for clinicians to anticipate these effects and to initiate measures to prevent or minimize them in order to maintain quality of life in prostate cancer survivors. Copyright

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L38 ANSWER 7 OF 16 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN  
ACCESSION NUMBER: 2003176120 EMBASE  
TITLE: RANK ligand and the regulation of skeletal remodeling.  
AUTHOR: Bell N.H.  
CORPORATE SOURCE: N.H. Bell, Department of Medicine, Medical University of South Carolina, 114 Doughty Street, Charleston, SC 29425, United States. belln@musc.edu  
SOURCE: Journal of Clinical Investigation, (2003) Vol. 111, No. 8, pp. 1120-1122.  
Refs: 24  
ISSN: 0021-9738 CODEN: JCINAO  
COUNTRY: United States  
DOCUMENT TYPE: Journal; Note  
FILE SEGMENT: 003 Endocrinology  
005 General Pathology and Pathological Anatomy  
006 Internal Medicine  
037 Drug Literature Index  
038 Adverse Reactions Titles  
LANGUAGE: English  
ENTRY DATE: Entered STN: 20030519  
Last Updated on STN: 20030519  
DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L38 ANSWER 8 OF 16 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN  
ACCESSION NUMBER: 2004038998 EMBASE  
TITLE: Overview of estrogen action in osteoblasts: Role of the ligand, the receptor, and the co-regulators.  
AUTHOR: Monroe D.G.; Secreto F.J.; Spelsberg T.C.  
CORPORATE SOURCE: Prof. T.C. Spelsberg, Dept. of Biochemistry/Molec. Biology, Mayo Clinic, 200 First Street SW, Rochester, MN 55905, United States. spelsberg.thomas@mayo.edu  
SOURCE: Journal of Musculoskeletal Neuronal Interactions, (2003) Vol. 3, No. 4, pp. 357-362.  
Refs: 40  
ISSN: 1108-7161 CODEN: JMNIB3  
COUNTRY: Greece  
DOCUMENT TYPE: Journal; General Review  
FILE SEGMENT: 030 Pharmacology  
033 Orthopedic Surgery  
037 Drug Literature Index  
038 Adverse Reactions Titles  
LANGUAGE: English  
ENTRY DATE: Entered STN: 20040220  
Last Updated on STN: 20040220  
DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L38 ANSWER 9 OF 16 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN  
DUPLICATE 3  
ACCESSION NUMBER: 2003:252884 BIOSIS  
DOCUMENT NUMBER: PREV200300252884  
TITLE: Lasofoxifene (CP-336, 156), a novel selective estrogen receptor modulator, in preclinical studies.  
AUTHOR(S): Ke, H. Z. [Reprint Author]; Brown, T. A.; Thompson, D. D.  
CORPORATE SOURCE: Osteoporosis Research, Groton Laboratories, Pfizer Global Research and Development, Mail Stop 8118W-216, Groton, CT, 06340, USA

SOURCE: huazhu ke@groton.pfizer.com  
Journal of the American Aging Association, (April 2002)  
Vol. 25, No. 2, pp. 87-100. print.  
DOCUMENT TYPE: Article  
General Review; (Literature Review)  
LANGUAGE: English  
ENTRY DATE: Entered STN: 28 May 2003  
Last Updated on STN: 28 May 2003

AB Estrogen replacement therapy is reported to reduce the incidence of vertebral fractures in postmenopausal women, however, its compliance is limited because of side effects and safety concerns. Estrogen's side effects on breast and uterine tissues leading to the potential increased risk of uterine and breast cancer limit widespread estrogen usage. Thus, there is a significant medical need for a therapy that protects against postmenopausal **bone loss** but is free of estrogen's negative effects on reproductive tissues. Selective estrogen receptor modulators (SERMs) have been investigated as an alternative to hormone replacement therapy. One such compound, **raloxifene**, has been approved for the prevention and treatment of **osteoporosis**. Lasofoxifene (LAS), a new, nonsteroidal, and potent SERM, is an estrogen antagonist or agonist depending on the target tissue. LAS selectively binds with high affinity to human estrogen receptors. In ovariectomized (OVX) rat studies, LAS prevented the decrease in femoral bone mineral density, tibial and lumbar vertebral trabecular bone mass at an ED100 of about 60 mug/kg/day. LAS inhibited the activation of trabecular and endocortical bone resorption and bone turnover in tibial metaphyses and diaphyses, and lumbar vertebral body in OVX rats. In addition, LAS decreased total serum cholesterol, inhibited body weight gain and increased soleus muscle weight in OVX rats. Similarly, LAS prevented **bone loss** induced by orchidectomy or aging in male rats by decreasing bone resorption and bone turnover while it had no effect in the prostate. Further, LAS decreased total serum cholesterol in intact aged male rats or in orchidectomized male rats. Synergistic skeletal effects were found with LAS in combination with bone anabolic agents such as prostaglandin E2 (**PGE2**), parathyroid hormone (PTH) or a growth hormone secretagogue (GHS) in OVX rats. In combination with estrogen, LAS inhibited the uterine stimulating effects of estrogen but did not block the bone protective effects of estrogen. In immature and aged female rats, LAS did not affect the uterine weight and uterine histology. In OVX adult female rats, LAS slightly but significantly increased uterine weight. These results demonstrated that LAS produced effects on the skeleton indistinguishable from estrogen in female and male rats. However, unlike estrogen, LAS had little effect on uterine weight and cellular proliferation of uterus in female rats. In preclinical anti-tumor studies, LAS inhibited human breast cancer growth in mice bearing MCF7 tumors, prevented NMU-induced mammary carcinomas and possessed chemotherapeutic effects in NMU-induced carcinomas in rats. Therefore, we conclude that LAS possesses the antiestrogenic effects in breast tissue and estrogenic effects in bone and serum cholesterol, but lacks estrogen's side effects on uterine tissue. These data support the therapeutic potential of LAS for the prevention and treatment of postmenopausal **bone loss** and mammary carcinomas in humans.

L38 ANSWER 10 OF 16 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 1999157824 EMBASE  
TITLE: [Advances in **osteoporosis** (V)].  
AVANCES EN **OSTEOPOROSIS** (V).  
AUTHOR: Seeman E.

CORPORATE SOURCE: E. Seeman, Endocrine Unit, Austin and Reparations Med.  
Centre, Studley Road, Heidlung, Vic. 3084, Australia  
SOURCE: Revista Espanola de Enfermedades Metabolicas Oseas, (1999)  
Vol. 8, No. 2, pp. 80-84.  
Refs: 38  
ISSN: 1132-8460 CODEN: REEOFC  
COUNTRY: Spain  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 031 Arthritis and Rheumatism  
037 Drug Literature Index  
LANGUAGE: Spanish  
ENTRY DATE: Entered STN: 19990520  
Last Updated on STN: 19990520  
DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L38 ANSWER 11 OF 16 MEDLINE on STN DUPLICATE 4  
ACCESSION NUMBER: 1999113821 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 9916783  
TITLE: **Droloxifene** does not blunt bone anabolic effects  
of prostaglandin E2, but maintains prostaglandin  
E2-restored bone in aged, ovariectomized rats.  
AUTHOR: Ke H Z; Crawford D T; Qi H; Pirie C M; Simmons H A;  
Chidsey-Frink K L; Chen H K; Jee W S; Thompson D D  
CORPORATE SOURCE: Department of Cardiovascular and Metabolic Diseases,  
Central Research Division, Pfizer Inc., Groton, CT 06340,  
USA.. huazhu\_ke@groton.pfizer.com  
SOURCE: Bone, (1999 Jan) 24 (1) 41-7.  
Journal code: 8504048. ISSN: 8756-3282.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals; Space Life Sciences  
ENTRY MONTH: 199903  
ENTRY DATE: Entered STN: 19990402  
Last Updated on STN: 20020124  
Entered Medline: 19990322  
AB **Droloxifene** (DRO) is a selective estrogen receptor modulator  
that prevents **bone loss** by inhibition of bone turnover  
associated with estrogen deficiency in both growing and aged female rats.  
The purposes of this study were to test: (a) whether DRO can maintain  
prostaglandin E2 (**PGE2**)-restored bone after discontinuation of  
**PGE2** in aged, ovariectomized (ovx) rats; (b) if an inhibition of  
bone turnover by DRO reduces bone anabolic effects of **PGE2**; and  
(c) whether bone mass restored by **PGE2** plus DRO can be  
maintained after discontinuation of both agents. Female rats at 12 months  
of age were sham-operated (sham) or ovx. Three months postsurgery, ovx  
rats were treated with either **PGE2** (3 mg/kg per day,  
subcutaneously [s.c.]) alone, or **PGE2** plus DRO (10 mg/kg per  
day, per os [p.o.]) for 2 months. Thereafter, the **PGE2** or  
**PGE2** plus DRO treatment was withdrawn and the rats were then  
treated with either vehicle or DRO for another 1.5 months. Using  
dual-energy X-ray absorptiometry (DXA), total lumbar vertebral bone  
mineral density (LV-BMD) was determined in vivo at months 0, 3, 5, and  
6.5. At the end of the study, the rats were autopsied, and BMD of total  
femur, femoral shaft, distal femoral metaphysis, and proximal femur was  
determined ex vivo by DXA. Standard static and dynamic bone  
histomorphometric parameters were determined on the fourth lumbar  
vertebral body (L-4). At 3, 5, or 6.5 months postsurgery, LV-BMD  
decreased significantly (-15%, -19%, and -19%, respectively) in the  
vehicle-treated ovx rats compared with sham. Beginning at 3 months



post-ovx, **PGE2** alone or in combination with DRO for 2 months completely restored LV-BMD back to the sham level. There was no difference in LV-BMD in **PGE2** alone or **PGE2** plus DRO. Upon cessation of **PGE2** treatment, a significant decrease in LV-BMD was observed in the **PGE2**-alone group (-12%). On the other hand, when DRO treatment was given after discontinuation of **PGE2**, the **PGE2**-restored LV-BMD was completely maintained. In the **PGE2** plus DRO group, no loss in LV-BMD was observed after cessation of either **PGE2** alone or both **PGE2** and DRO. However, treatment with DRO following 2 months of **PGE2** plus DRO further increased LV-BMD (+10%). At the end of the study, ex vivo femoral BMD data confirmed the observation in lumbar vertebrae. Histomorphometric results of L-4 indicated that loss in bone mass after cessation of **PGE2** in **PGE2** alone group was associated with increased bone turnover. Treatment with DRO in the maintenance phase inhibited bone turnover and prevented **bone loss** induced by withdrawal of **PGE2**. Trabecular bone mass was maintained in the **PGE2** plus DRO followed by vehicle group and further increased in the **PGE2** plus DRO followed by DRO groups. We found that: (a) DRO is efficacious in maintaining **PGE2**-restored bone after discontinuation of **PGE2**; (b) DRO did not blunt the anabolic effects of **PGE2**; (c) **bone loss** occurred after cessation of treatment in the **PGE2**-alone group, whereas it was maintained after cessation of treatment in **PGE2** plus DRO group; and (d) an additional anabolic effect was found in ovx rats treated with **PGE2** plus DRO followed by DRO.

L38 ANSWER 12 OF 16 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 1999030179 EMBASE  
 TITLE: Resveratrol stimulates the proliferation and differentiation of osteoblastic MC3T3-E1 cells.  
 AUTHOR: Mizutani K.; Ikeda K.; Kawai Y.; Yamori Y.  
 CORPORATE SOURCE: K. Mizutani, Dept Environmental Preservation Dev, Grad Sch Human Environmental Studies, Kyoto University, Yosida Nihonmatu-cho, Sakyo-hu, Kyoto 6068501, Japan  
 SOURCE: Biochemical and Biophysical Research Communications, (30 Dec 1998) Vol. 253, No. 3, pp. 859-863.  
 Refs: 37  
 ISSN: 0006-291X CODEN: BBRCA  
 COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article  
 FILE SEGMENT: 029 Clinical Biochemistry  
 037 Drug Literature Index  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 ENTRY DATE: Entered STN: 19990128  
 Last Updated on STN: 19990128

AB Nutritional and pharmacological factors are needed to prevent **bone loss** that occurs with increasing age. The chemical compounds that act on bone metabolism as nutrients in food, however, are poorly understood. The effect of resveratrol, a natural phytoestrogen, on the proliferation and differentiation of osteoblastic MC3T3-E1 cells was studied. Resveratrol dose-dependently increased DNA synthesis ( $10^{-9}$  -  $10^{-7}$  M) of MC3T3-E1 cells. In addition, resveratrol increased alkaline phosphatase (ALP) activity and prolyl hydroxylase activity of MC3T3-E1 cells ( $10^{-6}$  -  $10^{-5}$  M). Moreover, the antiestrogen **tamoxifen** eliminated the stimulation of MC3T3-E1 cells on the proliferation and ALP activity by resveratrol. On the other hand, resveratrol inhibited prostaglandin E2 production in MC3T3-E1 cells ( $10^{-8}$  -  $10^{-6}$  M). Our

present study is the first to demonstrate that resveratrol directly stimulates cell proliferation and differentiation of osteoblasts.

L38 ANSWER 13 OF 16 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 95182904 EMBASE  
DOCUMENT NUMBER: 1995182904  
TITLE: **Tamoxifen**: Oestrogen or anti-oestrogen in bone?.  
AUTHOR: Wright C.D.P.; Compston J.E.  
CORPORATE SOURCE: Department of Medicine, Addenbrooke's Hospital, Cambridge CB2 2QQ, United Kingdom  
SOURCE: QJM - Monthly Journal of the Association of Physicians, (1995) Vol. 88, No. 5, pp. 307-310.  
ISSN: 0033-5622 CODEN: QMJPFH  
COUNTRY: United Kingdom  
DOCUMENT TYPE: Journal; (Short Survey)  
FILE SEGMENT: 003 Endocrinology  
006 Internal Medicine  
016 Cancer  
030 Pharmacology  
037 Drug Literature Index  
LANGUAGE: English  
ENTRY DATE: Entered STN: 950707  
Last Updated on STN: 950707

DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L38 ANSWER 14 OF 16 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 95275413 EMBASE  
DOCUMENT NUMBER: 1995275413  
TITLE: Present and future of **osteoporosis** therapy.  
AUTHOR: Seeman E.; Tsalamandris C.; Bass S.; Pearce G.  
CORPORATE SOURCE: Endocrine Department, Austin Hospital, Heidelberg, Melbourne 3084, Australia  
SOURCE: Bone, (1995) Vol. 17, No. 2 SUPPL., pp. 23S-29S.  
ISSN: 8756-3282 CODEN: BONEDL  
COUNTRY: United States  
DOCUMENT TYPE: Journal; Conference Article  
FILE SEGMENT: 033 Orthopedic Surgery  
037 Drug Literature Index  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ENTRY DATE: Entered STN: 951003  
Last Updated on STN: 951003

AB In the 50-year 'modern' history of **osteoporosis**, there have been about 17 antifracture studies with sufficient attention to design to allow inference regarding efficacy. Antivertebral fracture efficacy has been reported with etidronate, estrogen patch, calcitonin, and 1,25-dihydroxyvitamin D. Two studies using fluoride were positive, and two were negative. Hip fractures have been neglected. One study showed efficacy of hip protectors, one showed efficacy of vitamin D and calcium in nursing home dwellers. The source of most hip fractures is the community. One community based antihip fracture efficacy study using annual injections of vitamin D was positive. There have been no antivertebral or antihip fracture studies in men, or in corticosteroid-related **osteoporosis** in men or women. Lack of independently repeated demonstration of efficacy, small fracture numbers, and data pooling in some of these (the best) studies leave great uncertainty. Estrogen and bisphosphonates appear to be the best options at this time. New data suggest that calcium supplementation is likely to

reduce the rate of **bone loss** and perhaps reduce fracture rates. The challenge is to maintain and restore the constituents of bone mineral density (BMD), that is: to promote periosteal and endosteal bone formation; reduce endosteal bone resorption and cortical porosity; and increase trabecular thickness, number, and connectivity. There are many opportunities, for instance, intermittent parathyroid hormone (PTH) increases bone strength and, with estrogen, may increase connectivity. The anabolic effects of PTH may be partly mediated by IGF-1. IGF-1 increases periosteal, endosteal, and trabecular bone formation, cortical and trabecular width, and trabecular and endocortical connectivity. With bisphosphonate, IGF-1 may increase bone area and strength as the bisphosphonate decreases medullary area while IGF-1 increases subperiosteal area. Anabolic effects of fluoride warrant further study provided that the study design addresses the issue of bone strength, the narrow toxic-therapeutic window, and cortical **bone loss**. Aluminum, a constituent of zeolite, has anabolic effects which may be partly mediated by TGF- $\beta$ . Prostaglandin E2 increases periosteal and endosteal bone formation but may increase cortical porosity. More data are needed regarding these growth factors, silicon compounds, strontium salts, and flavonoids. The effects of medroxyprogesterone and 19 norprogestins on BMD have not been compared. **Raloxifene**, a new estrogen agonist free of endometrial hyperplastic effects, is being studied. Most treated individuals with **osteoporosis** (i.e., low BMD with or without a fracture) will not suffer a fracture so treatment must be safe. Success - absence of fracture - will be measured by the epidemiologist because it is difficult to distinguish efficacy from chance in an individual as the peak incidence of fractures in the community is usually only about 1-4/100 per year.

L38 ANSWER 15 OF 16 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 93314365 EMBASE  
 DOCUMENT NUMBER: 1993314365  
 TITLE: Menopause.  
 AUTHOR: Dawood M.Y.; Tidey G.F.  
 CORPORATE SOURCE: Div. of Reproductive Endocrinology, Department of Reproductive Sciences, University of Texas Medical School, Houston, TX, United States  
 SOURCE: Current Problems in Obstetrics, Gynecology and Fertility, (1993) Vol. 16, No. 5, pp. 172-207.  
 ISSN: 8756-0410 CODEN: CPOIEN  
 COUNTRY: United States  
 DOCUMENT TYPE: Journal; (Short Survey)  
 FILE SEGMENT: 010 Obstetrics and Gynecology  
 016 Cancer  
 037 Drug Literature Index  
 038 Adverse Reactions Titles  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 ENTRY DATE: Entered STN: 931121  
 Last Updated on STN: 931121  
 AB Menopause is best viewed as an endocrinopathy characterized by ovarian hypofunction, which results in a deficiency of estrogen and progesterone. Other syndromes of endocrine hypofunction, such as hypothyroidism or hypoadrenalism, result in acute clinical syndromes necessitating urgent physiologic replacement of the deficient hormone; however, the focus of hormone replacement therapy after the menopause is primarily health maintenance and prevention of chronic disease. Accordingly, protection against cardiovascular disease is now the primary indication for estrogen replacement, because this leading cause of mortality in women can be

reduced by half in estrogen users. Although smaller in magnitude, a substantial reduction in **osteoporosis**-related morbidity and mortality is also enjoyed by menopausal women who receive estrogen. Given these considerable benefits, an increasingly important mission of the primary care physician over the next decade is to ensure that appropriate hormone replacement therapy is given to most women who suffer from this endocrinopathy. Like many other interventions for health maintenance and disease prevention, hormone replacement has received a lukewarm response from many patients and some physicians. This is in part because of the unwanted and sometimes unexpected side effect of persistent bleeding as well as a fear of increased risk of cancer, which has received excessive media coverage but is largely unjustified. We therefore review both basic and clinical studies that support the overwhelming benefits of estrogen replacement in menopausal women. More important, however, we discuss new hormone replacement regimens that minimize the incidence of unwanted vaginal bleeding, and we review the controversial literature on breast cancer risk in estrogen users. Finally, alternatives to standard hormone replacement regimens for women with contraindications to estrogen therapy are discussed.

L38 ANSWER 16 OF 16 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 1986:164818 BIOSIS  
DOCUMENT NUMBER: PREV198681075234; BA81:75234  
TITLE: EFFECTS OF THE ANTIESTROGENS **TAMOXIFEN** AND CLOMIPHENE ON BONE RESORPTION IN-VITRO.  
AUTHOR(S): STEWARD P J [Reprint author]; STERN P H  
CORPORATE SOURCE: DEP PHARMACOL, NORTHWEST UNIV, 303 EAST CHICAGO AVE, CHICAGO, ILL 60611, USA  
SOURCE: Endocrinology, (1986) Vol. 118, No. 1, pp. 125-131.  
CODEN: ENDOAO. ISSN: 0013-7227.  
DOCUMENT TYPE: Article  
FILE SEGMENT: BA  
LANGUAGE: ENGLISH  
ENTRY DATE: Entered STN: 26 Apr 1986  
Last Updated on STN: 26 Apr 1986

AB The in vitro effect of the nonsteroidal antiestrogens **tamoxifen** (TAM) and clomiphene (CLO) on bone resorption was investigated. TAM (100  $\mu$ M) and CLO (100  $\mu$ M) completely blocked PTH (2 nM)-induced resorption; 10  $\mu$ M TAM was ineffective in blocking resorption, while 40-50  $\mu$ M partially inhibited the response. TAM (100  $\mu$ M) also completely blocked prostaglandin E2 (30 nM)- and 1,25-dihydroxy vitamin D3 (0.5 nM)-induced bone resorption. A 16-h pretreatment with TAM blocked subsequent stimulation of resorption by PTH, whereas 3.5- or 7-h pretreatment with antiestrogen was ineffective in blocking the response. Both protein and DNA syntheses were inhibited by continuous treatment (48 h) with the antiestrogens. When antiestrogen-pretreated (16 h) bones were transferred to fresh medium not containing antiestrogen, protein and DNA syntheses recovered to approximately half the control (nonantiestrogen-treated) values within 48 h. Bone resorption, however, was still completely inhibited even though macromolecular synthesis had substantially recovered. Thus, mechanisms other than macromolecular synthesis inhibition could be involved in the inhibition of bone resorption by the nonsteroidal antiestrogens TAM and CLO.

=&gt; d que stat 139

L26 4 SEA FILE=REGISTRY ABB=ON (82413-20-5 OR 84449-90-1 OR  
 10540-29-1 OR 68047-06-3)/RN  
 L27 7 SEA FILE=REGISTRY ABB=ON (180915-84-8 OR 180915-78-0 OR  
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 180916-15-8)/RN  
 L28 11 SEA FILE=REGISTRY ABB=ON L26 OR L27  
 L29 4 SEA FILE=REGISTRY ABB=ON (PGD1 OR PGD2 OR PGE2 OR PGE1 OR  
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 L30 1 SEA FILE=REGISTRY ABB=ON PGF2A/CN  
 L31 5 SEA FILE=REGISTRY ABB=ON L29 OR L30  
 L32 6 SEA FILE=REGISTRY ABB=ON L31 OR 195962-24-4/RN  
 L33 10983 SEA FILE=HCAPLUS ABB=ON L28 OR ?DROLOXIFENE? OR ?RALOXIFENE?  
 OR ?TAMOXIFEN?  
 L34 73 SEA FILE=HCAPLUS ABB=ON L33 AND (L32 OR PGD1 OR PGD2 OR PGE2  
 OR PGE1 OR PGF2 OR PGF2A OR PGF2A)  
 L35 6 SEA FILE=HCAPLUS ABB=ON L34 AND (?BONE?(W)(?LOSS? OR ?LOSE?  
 OR ?RESORP) OR ?OSTEOPOROS? OR ?PAGET?)  
 L39 1 SEA FILE=USPATFULL ABB=ON L35 AND (PRD<19960228 OR PD<19960228  
 )

=&gt; d ibib abs 139 1

L39 ANSWER 1 OF 1 USPATFULL on STN

ACCESSION NUMBER: 2001:121585 USPATFULL  
 TITLE: Intracellular vitamin D binding protein  
 INVENTOR(S): Adams, John S., Los Angeles, CA, United States  
 PATENT ASSIGNEE(S): Cedars-Sinai Medical Center, Los Angeles, CA, United  
 States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6268478	B1	20010731
APPLICATION INFO.:	US 1997-797358		19970211 (8)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1996-11491P	19960212 (60) <--
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	GRANTED	
PRIMARY EXAMINER:	Kunz, Gary L.	
ASSISTANT EXAMINER:	O'Hara, Eileen B.	
LEGAL REPRESENTATIVE:	Campbell & Flores LLP	
NUMBER OF CLAIMS:	27	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	11 Drawing Figure(s); 11 Drawing Page(s)	
LINE COUNT:	1597	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to the discovery and purification of novel  
 intracellular vitamin D binding proteins (IDBPs) and the isolation of  
 polynucleotide sequences encoding the proteins. IDBPs are of interest  
 because they mediate the vitamin D resistance, i.e., insensitivity,  
 observed in new world primates. IDBPs are distinct from the vitamin D  
 receptor and other intracellular receptors, e.g. estrogen receptor. One  
 aspect of the invention is to provide purified IDBPs as pharmaceutical  
 compositions to affect steroid hormone activity. Another aspect of the  
 invention provides polynucleotides encoding the IDBPs of the invention  
 for use in altering the expression of IDBPs. Yet another aspect of the  
 invention is to provide assays for the detection or screening of  
 therapeutic compounds that interfere with the interaction between IDBP

and vitamin D (or other ligands that bind to IDBP), and the use of such compounds as pharmaceutical compositions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Leith 09/736,051

14/10/2005

=&gt; d ibib abs ind hitstr l15 1-5

L15 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:811078 HCAPLUS

DOCUMENT NUMBER: 132:45000

TITLE: Therapeutic combinations of (selective) estrogen receptor modulators (SERM) and growth hormone secretagogues (GHS) for treating musculoskeletal frailty

INVENTOR(S): Ke, Hua Zhu; Li, Mei; Pan, Lydia Codetta; Thompson, David Duane

PATENT ASSIGNEE(S): Pfizer Products Inc., USA

SOURCE: PCT Int. Appl., 31 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9965488	A1	19991223	WO 1999-IB796	19990503
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
CA 2335112	AA	19991223	CA 1999-2335112	19990503
AU 9933420	A1	20000105	AU 1999-33420	19990503
BR 9911357	A	20010313	BR 1999-11357	19990503
EP 1085867	A1	20010328	EP 1999-914723	19990503
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO			
JP 2002518328	T2	20020625	JP 2000-554368	19990503
ZA 9903973	A	20001215	ZA 1999-3973	19990615
NO 2000006381	A	20001214	NO 2000-6381	20001214
HR 2000000857	A1	20011031	HR 2000-857	20001214
BG 105128	A	20011130	BG 2001-105128	20010108
PRIORITY APPLN. INFO.:			US 1998-89424P	P 19980616
			WO 1999-IB796	W 19990503

AB This invention is directed to pharmaceutical combination compns. and methods comprising (-)-cis-6-phenyl-5-(4-(2-pyrrolidin-1-yl-ethoxy)phenyl)-5,6,7,8-tetrahydronaphthalene-2-ol or a pharmaceutically acceptable salt thereof and 2-amino-N-(1(R)-(2,4-difluorobenzyloxymethyl)-2-oxo-2-(3-oxo-3a(R)pyridin-2-ylmethyl)-2-(2,2,2-trifluoroethyl)-2,3,3a,4,6,7-hexahydropyrazolo[4,3-c]pyridin-5-yl)ethyl-2-methylpropionamide or a pharmaceutically acceptable salt thereof, methods of using such compns. and kits containing such compns. The compns. are useful for treating musculoskeletal frailty, including **osteoporosis**, **osteoporotic** fracture, low bone mass, frailty and low muscle mass.

IC ICM A61K031-44

CC 1-12 (Pharmacology)

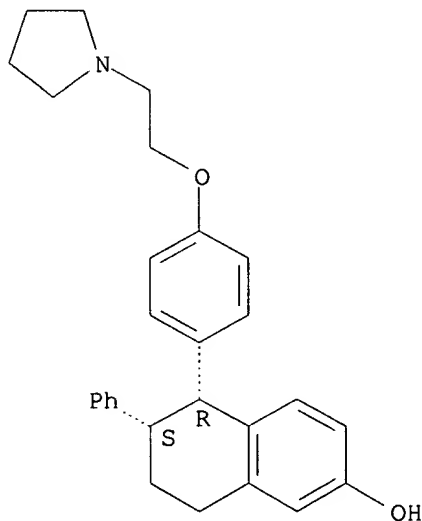
ST **osteoporosis** estrogen receptor growth hormone; periodontitis  
estrogen receptor modulator growth hormone; **bone loss**  
estrogen receptor growth hormone

IT Periodontium

(periodontitis; therapeutic combinations of estrogen receptor

- modulators and growth hormone secretagogues for treating musculoskeletal frailty)
- IT Bone  
(resorption; therapeutic combinations of estrogen receptor modulators and growth hormone secretagogues for treating musculoskeletal frailty)
- IT **Osteoporosis**  
(therapeutic agents; therapeutic combinations of estrogen receptor modulators and growth hormone secretagogues for treating musculoskeletal frailty)
- IT Estrogen receptors  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(therapeutic combinations of estrogen receptor modulators and growth hormone secretagogues for treating musculoskeletal frailty)
- IT **180916-16-9 190791-29-8 193272-70-7 218163-71-4**  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(therapeutic combinations of estrogen receptor modulators and growth hormone secretagogues for treating musculoskeletal frailty)
- IT **9002-72-6**, Growth hormone  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(therapeutic combinations of estrogen receptor modulators and growth hormone secretagogues for treating musculoskeletal frailty)
- IT **180916-16-9 190791-29-8 193272-70-7 218163-71-4**  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(therapeutic combinations of estrogen receptor modulators and growth hormone secretagogues for treating musculoskeletal frailty)
- RN 180916-16-9 HCAPLUS
- CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 190791-29-8 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-



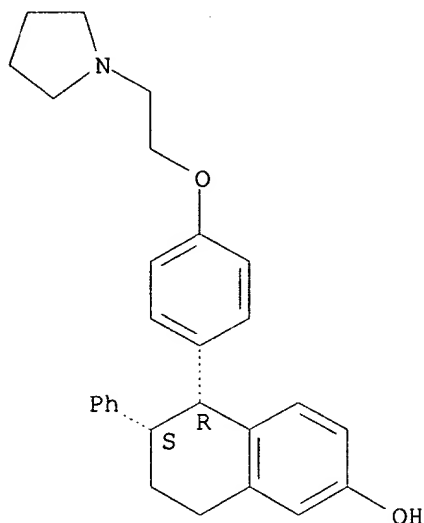
pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)-, (2S,3S)-2,3-dihydroxybutanedioate  
(1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 180916-16-9

CMF C28 H31 N O2

Absolute stereochemistry. Rotation (-).

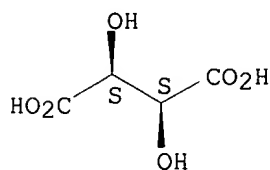


CM 2

CRN 147-71-7

CMF C4 H6 O6

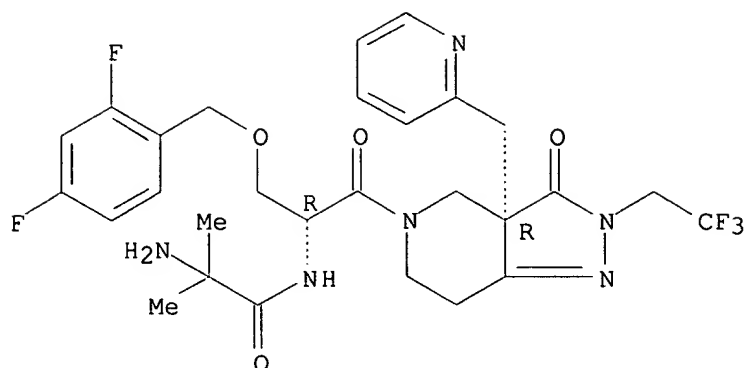
Absolute stereochemistry.



RN 193272-70-7 HCAPLUS

CN Propanamide, 2-amino-N-[(1R)-1-[(2,4-difluorophenyl)methoxy)methyl]-2-  
[(3aR)-2,3,3a,4,6,7-hexahydro-3-oxo-3a-(2-pyridinylmethyl)-2-(2,2,2-  
trifluoroethyl)-5H-pyrazolo[4,3-c]pyridin-5-yl]-2-oxoethyl]-2-methyl-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 218163-71-4 HCAPLUS

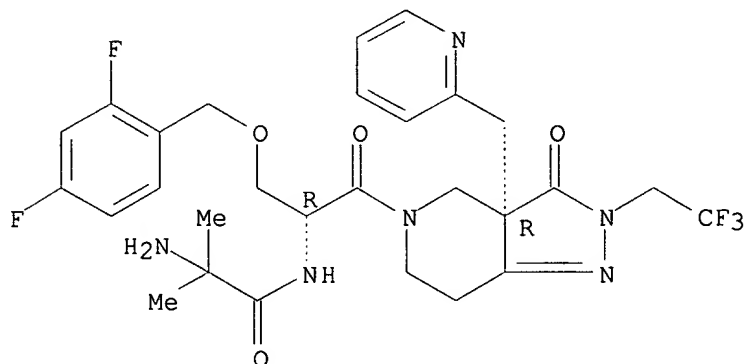
CN Propanamide, 2-amino-N-[(1R)-1-[[2,4-difluorophenyl)methoxy)methyl]-2-[(3aR)-2,3,3a,4,6,7-hexahydro-3-oxo-3a-(2-pyridinylmethyl)-2-(2,2,2-trifluoroethyl)-5H-pyrazolo[4,3-c]pyridin-5-yl]-2-oxoethyl]-2-methyl-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 193272-70-7

CMF C28 H31 F5 N6 O4

Absolute stereochemistry.

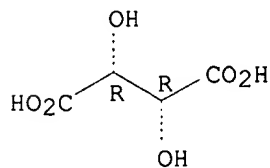


CM 2

CRN 87-69-4

CMF C4 H6 O6

Absolute stereochemistry.



IT 9002-72-6, Growth hormone  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(therapeutic combinations of estrogen receptor modulators and growth  
hormone secretagogues for treating musculoskeletal frailty)  
RN 9002-72-6 HCAPLUS  
CN Somatotropin (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:450913 HCAPLUS

DOCUMENT NUMBER: 129:184100

TITLE: Discovery and Preclinical Pharmacology of a Novel,  
Potent, Nonsteroidal Estrogen Receptor  
Agonist/Antagonist, CP-336156, a  
Diaryltetrahydronaphthalene

AUTHOR(S): Rosati, Robert L.; Jardine, Paul Da Silva; Cameron,  
Kimberly O.; **Thompson, David D.**; **Ke,**  
**Hua Zhu**; Toler, Steven M.; Brown, Thomas A.; Pan,  
Lydia C.; Ebbinghaus, Charles F.; Reinhold, Anthony  
R.; Elliott, Nancy C.; Newhouse, Bradley N.; Tjoa,  
Christina M.; Sweetnam, Paul M.; Cole, Mark J.;  
Arriola, Mark W.; Gauthier, Jeffrey W.; Crawford, D.  
Todd; Nickerson, David F.; Pirie, Christine M.; Qi,  
Hong; Simmons, Hollis A.; Tkalcovic, George T.

CORPORATE SOURCE: Central Research Division, Pfizer Inc., Groton, CT,  
06340, USA

SOURCE: Journal of Medicinal Chemistry (1998), 41(16),  
2928-2931

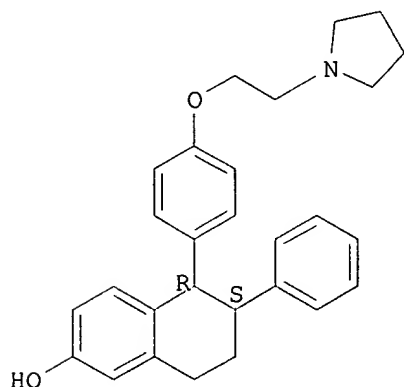
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



I

AB CP-336156 (I), a nonsteroidal estrogen agonist/antagonist with excellent oral bioavailability, was prepared and is as potent and efficacious as estrogen at preventing **bone loss** and lowering total serum cholesterol in rats. In addition, estrogen-like proliferative effects on breast and uterine tissue were not observed. The superior oral kinetics,

achieved by minimizing intestinal glucuronidation through the application of a structural model, translated into a breakthrough for in vivo potency.

CC 1-10 (Pharmacology)  
Section cross-reference(s): 25, 27

ST CP336156 estrogen agonist antagonist tetrahydronaphthalene

IT Estrogens  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(antiestrogens; preparation and preclin. pharmacol. of a potent, nonsteroidal estrogen agonist/antagonist, CP-336156)

IT Anticholesteremic agents  
Drug bioavailability  
**Osteoporosis**  
(preparation and preclin. pharmacol. of a potent, nonsteroidal estrogen agonist/antagonist, CP-336156)

IT Estrogens  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(preparation and preclin. pharmacol. of a potent, nonsteroidal estrogen agonist/antagonist, CP-336156)

IT 50-28-2, 17 $\beta$ -Estradiol, biological studies 84449-90-1  
, Raloxifene 211797-30-7  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(preparation and preclin. pharmacol. of a potent, nonsteroidal estrogen agonist/antagonist, CP-336156)

IT 1845-11-0  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)  
(preparation and preclin. pharmacol. of a potent, nonsteroidal estrogen agonist/antagonist, CP-336156)

IT 4796-75-2P 180915-96-2P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)  
(preparation and preclin. pharmacol. of a potent, nonsteroidal estrogen agonist/antagonist, CP-336156)

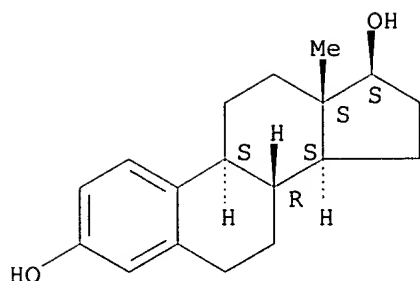
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180915-93-9P 180916-16-9P, 2-Naphthalenol,  
5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-,  
(5R,6S)- 190791-29-8P, CP-336156  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(preparation and preclin. pharmacol. of a potent, nonsteroidal estrogen agonist/antagonist, CP-336156)

IT 50-28-2, 17 $\beta$ -Estradiol, biological studies 84449-90-1  
, Raloxifene 211797-30-7  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(preparation and preclin. pharmacol. of a potent, nonsteroidal estrogen agonist/antagonist, CP-336156)

RN 50-28-2 HCAPLUS

CN Estra-1,3,5(10)-triene-3,17-diol (17 $\beta$ )- (9CI) (CA INDEX NAME)

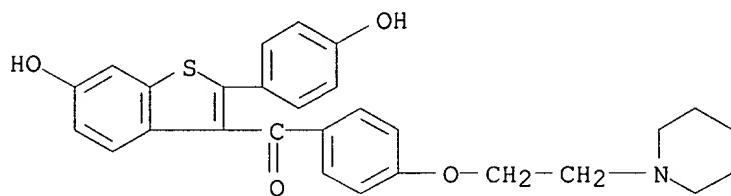
Absolute stereochemistry.



RN 84449-90-1 HCAPLUS

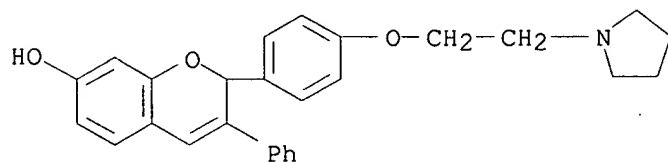
CN Methanone, [6-hydroxy-2-(4-hydroxyphenyl)benzo[b]thien-3-yl][4-[2-(1-piperidinyl)ethoxy]phenyl]- (9CI) (CA INDEX NAME)

② Raloxiprone



RN 211797-30-7 HCAPLUS

CN 2H-1-Benzopyran-7-ol, 3-phenyl-2-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]- (9CI) (CA INDEX NAME)



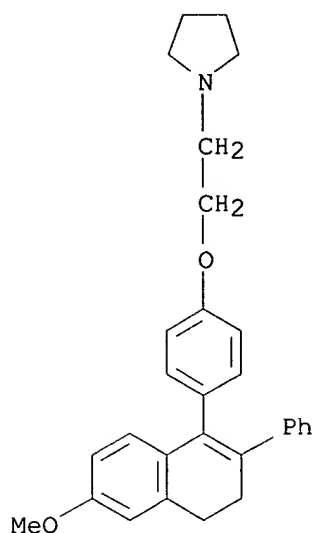
IT 1845-11-0

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)

(preparation and preclin. pharmacol. of a potent, nonsteroidal estrogen agonist/antagonist, CP-336156)

RN 1845-11-0 HCAPLUS

CN Pyrrolidine, 1-[2-[4-(3,4-dihydro-6-methoxy-2-phenyl-1-naphthalenyl)phenoxy]ethyl]- (9CI) (CA INDEX NAME)



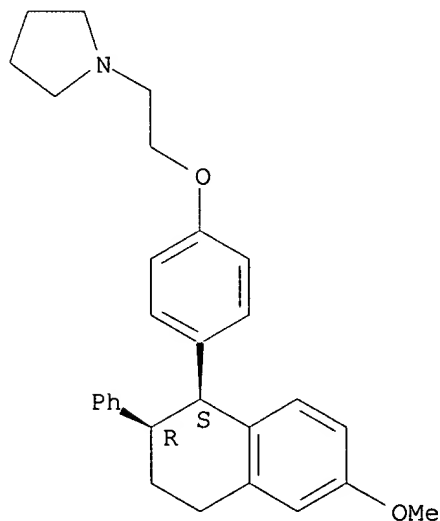
IT 4796-75-2P 180915-96-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent) (preparation and preclin. pharmacol. of a potent, nonsteroidal estrogen agonist/antagonist, CP-336156)

RN 4796-75-2 HCAPLUS

CN Pyrrolidine, 1-[2-[4-[(1R,2S)-1,2,3,4-tetrahydro-6-methoxy-2-phenyl-1-naphthalenyl]phenoxy]ethyl]-, rel- (9CI) (CA INDEX NAME)

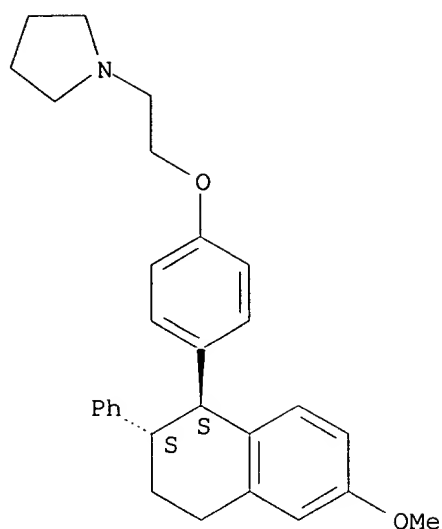
Relative stereochemistry.



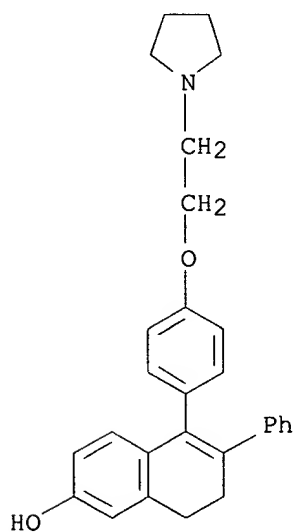
RN 180915-96-2 HCAPLUS

CN Pyrrolidine, 1-[2-[4-[(1R,2R)-1,2,3,4-tetrahydro-6-methoxy-2-phenyl-1-naphthalenyl]phenoxy]ethyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

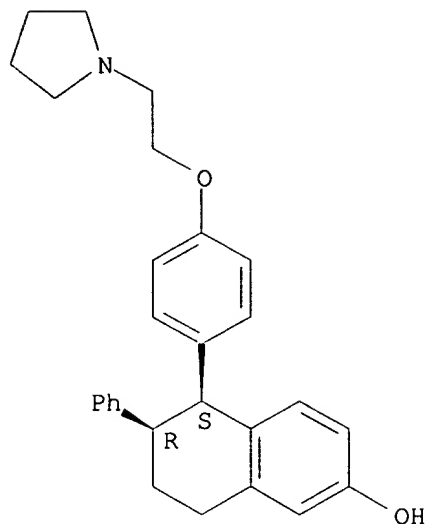


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 180915-93-9P 180916-16-9P, 2-Naphthalenol,  
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 (5R,6S)- 190791-29-8P, CP-336156  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
 study, unclassified); SPN (Synthetic preparation); BIOL (Biological  
 study); PREP (Preparation)  
 (preparation and preclin. pharmacol. of a potent, nonsteroidal estrogen  
 agonist/antagonist, CP-336156)  
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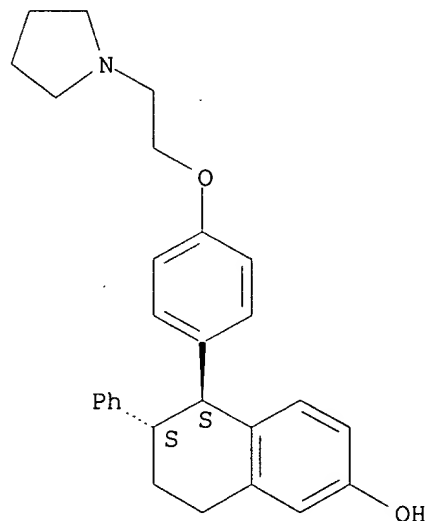
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Relative stereochemistry.



RN 180915-79-1 HCAPLUS  
 CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6R)-rel- (9CI) (CA INDEX NAME)

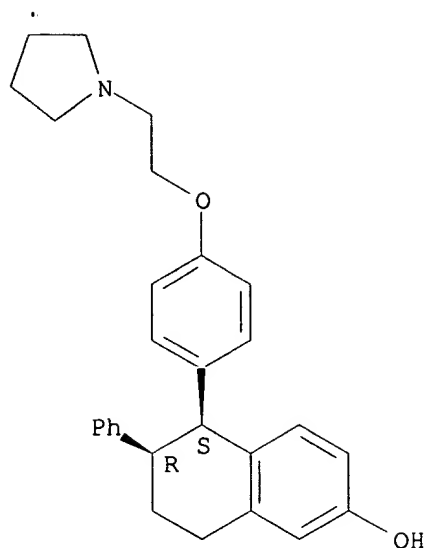
Relative stereochemistry.



RN 180915-93-9 HCAPLUS  
 CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5S,6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

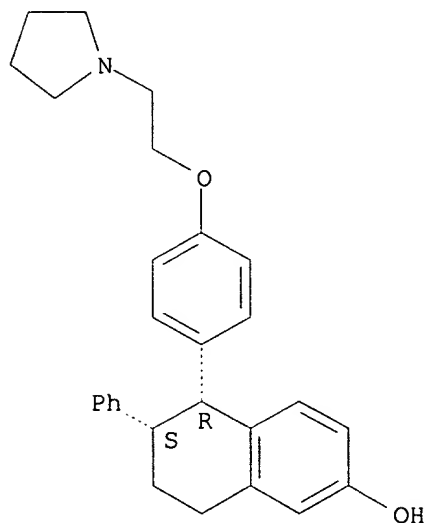




RN 180916-16-9 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 190791-29-8 HCAPLUS

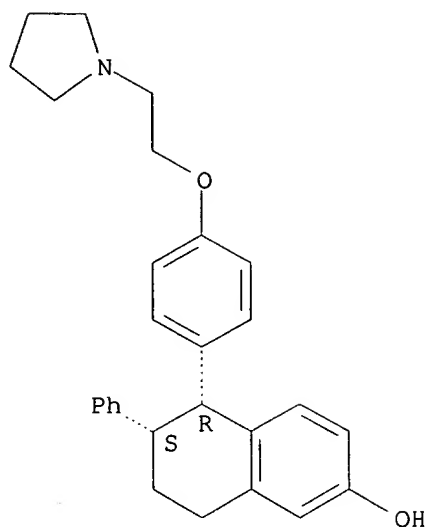
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)-, (2S,3S)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

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CRN 180916-16-9

CMF C28 H31 N O2

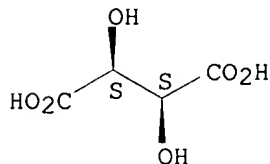
Absolute stereochemistry. Rotation (-).



CM 2

CRN 147-71-7  
CMF C4 H6 O6

Absolute stereochemistry.



REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1997:594636 HCAPLUS

DOCUMENT NUMBER: 127:257642

TITLE: Combination therapy for **osteoporosis** with  
estrogen agonists/antagonists and prostaglandins or  
prostaglandin agonists/antagonists

INVENTOR(S): **Ke, Hua Zhu; Thompson, David D.**

PATENT ASSIGNEE(S): Pfizer Inc., USA

SOURCE: PCT Int. Appl., 78 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9731640	A1	19970904	WO 1996-IB1462	19961223
W: AU, BG, BR, BY, CA, CN, CZ, HU, IL, IS, JP, KR, KZ, LK, LV, MX,				

NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, US, UZ, VN  
 RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT,  
 SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

TW 464496	B	20011121	TW 1996-85115770	19961220
CA 2247420	AA	19970904	CA 1996-2247420	19961223
AU 9710398	A1	19970916	AU 1997-10398	19961223
AU 703285	B2	19990325		
EP 883404	A1	19981216	EP 1996-941153	19961223
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LV, FI, RO				
CN 1209064	A	19990224	CN 1996-180058	19961223
JP 11504352	T2	19990420	JP 1997-530738	19961223
BR 9612533	A	19990720	BR 1996-12533	19961223
NZ 323456	A	20010330	NZ 1996-323456	19961223
TR 9801679	T2	20010621	TR 1998-9801679	19961223
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JP 2002308771	A2	20021023	JP 2002-54756	19961223
PL 187219	B1	20040630	PL 1996-328831	19961223
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CN 1515317	A	20040728	CN 2003-10120235	19961223
CN 1515258	A	20040728	CN 2003-10120236	19961223
PL 187962	B1	20041130	PL 1996-359987	19961223
ZA 9701719	A	19980827	ZA 1997-1719	19970227
AP 975	A	20010612	AP 2000-200001962	19970227
W: BW, GM, KE, MW, UG, ZM, ZW				
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US 6323232	B1	20011127	US 1998-117972	19980811
NO 9803936	A	19980827	NO 1998-3936	19980827
US 2001009920	A1	20010726	US 2000-736051	20001213
AP 1179	A	20030630	AP 2002-2661	20021107
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PRIORITY APPLN. INFO.:			US 1996-12412P	P 19960228
			EP 1996-941153	A3 19961223
			JP 1997-530738	A3 19961223
			WO 1996-IB1462	W 19961223
			US 1998-117972	A3 19980811

OTHER SOURCE(S): MARPAT 127:257642

AB Pharmaceutical combination compns. are disclosed which include estrogen agonists/antagonists and prostaglandins or prostaglandin agonists/antagonists. The compns. are useful for the treatment of bone disorders including **osteoporosis**. The effects of PGE2 and droloxifene on bone mineral content and bone mineral d. in ovariectomized rats were determined. The data support the strategy of using an anabolic agent to restore bone mass, followed by an anti-resorptive agent to maintain the restored bone mass.

IC ICM A61K031-557

ICS A61K031-135; A61K031-38; A61K033-16; A61K038-29; A61K038-27;  
 A61K038-00; A61K031-445; A61K031-557; A61K031-135; A61K031-38;  
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 A61K031-38; A61K038-27; A61K031-135; A61K031-38

CC 1-12 (Pharmacology)

Section cross-reference(s): 2, 63

ST **osteoporosis** estrogen agonist antagonist prostaglandin  
 combination; agonist antagonist estrogen prostaglandin bone disorder

- IT Estrogens  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (antiestrogens; estrogen agonists/antagonists and prostaglandins or prostaglandin agonists/antagonists as combination therapy for bone disorders including **osteoporosis**)
- IT Bone, disease  
 Bone formation  
 Drug delivery systems  
**Osteoporosis**  
 (estrogen agonists/antagonists and prostaglandins or prostaglandin agonists/antagonists as combination therapy for bone disorders including **osteoporosis**)
- IT Estrogens  
 Prostaglandins  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (estrogen agonists/antagonists and prostaglandins or prostaglandin agonists/antagonists as combination therapy for bone disorders including **osteoporosis**)
- IT Prostaglandins  
 Prostaglandins  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (inhibitors; estrogen agonists/antagonists and prostaglandins or prostaglandin agonists/antagonists as combination therapy for bone disorders including **osteoporosis**)
- IT Bone  
 (resorption, inhibitors; estrogen agonists/antagonists and prostaglandins or prostaglandin agonists/antagonists as combination therapy for bone disorders including **osteoporosis**)
- IT Drug interactions  
 (synergistic; estrogen agonists/antagonists and prostaglandins or prostaglandin agonists/antagonists as combination therapy for bone disorders including **osteoporosis**)
- IT Drug delivery systems  
 (unit doses; estrogen agonists/antagonists and prostaglandins or prostaglandin agonists/antagonists as combination therapy for bone disorders including **osteoporosis**)
- IT 9002-72-6, Growth hormone  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (and growth hormone secretagogues; estrogen agonists/antagonists and prostaglandins or prostaglandin agonists/antagonists as combination therapy for bone disorders including **osteoporosis**)
- IT 363-24-6, PGE2 551-11-1, PGF2 $\alpha$  745-65-3,  
 PGE1 7681-49-4, Sodium fluoride, biological studies  
 9002-64-6, Parathyroid hormone 10540-29-1, Tamoxifen  
 17968-82-0, PGD1 31477-60-8, Centchroman  
 41598-07-6, PGD2 68047-06-3, 4-Hydroxytamoxifen  
 82413-20-5, Droloxifene 84449-90-1, Raloxifene  
 116057-75-1, Idoxifene 123123-44-4 159752-10-0  
 , MK-677 180915-78-0 180915-84-8 180915-86-0  
 180916-14-7 180916-15-8 180916-16-9  
 193274-89-4 195962-24-4  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(estrogen agonists/antagonists and prostaglandins or prostaglandin agonists/antagonists as combination therapy for bone disorders including **osteoporosis**)

IT 9002-72-6, Growth hormone

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(and growth hormone secretagogues; estrogen agonists/antagonists and prostaglandins or prostaglandin agonists/antagonists as combination therapy for bone disorders including **osteoporosis**)

RN 9002-72-6 HCAPLUS

CN Somatotropin (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

IT 363-24-6, PGE2 551-11-1, PGF2 $\alpha$  745-65-3,  
PGE1 7681-49-4, Sodium **fluoride**, biological studies  
9002-64-6, Parathyroid hormone 10540-29-1, Tamoxifen  
17968-82-0, PGD1 31477-60-8, Centchroman  
41598-07-6, PGD2 68047-06-3, 4-Hydroxytamoxifen  
82413-20-5, Droloxifene 84449-90-1, Raloxifene  
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, MK-677 180915-78-0 180915-84-8 180915-86-0  
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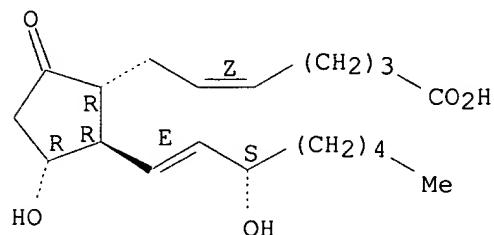
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(estrogen agonists/antagonists and prostaglandins or prostaglandin agonists/antagonists as combination therapy for bone disorders including **osteoporosis**)

RN 363-24-6 HCAPLUS

CN Prosta-5,13-dien-1-oic acid, 11,15-dihydroxy-9-oxo-,  
(5Z,11 $\alpha$ ,13E,15S)- (9CI) (CA INDEX NAME)

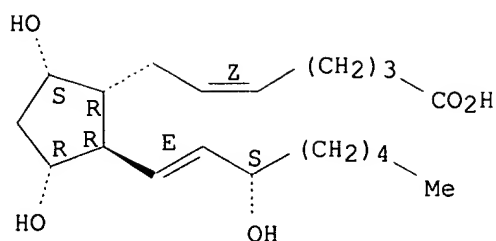
Absolute stereochemistry.  
Double bond geometry as shown.



RN 551-11-1 HCAPLUS

CN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-,  
(5Z,9 $\alpha$ ,11 $\alpha$ ,13E,15S)- (9CI) (CA INDEX NAME)

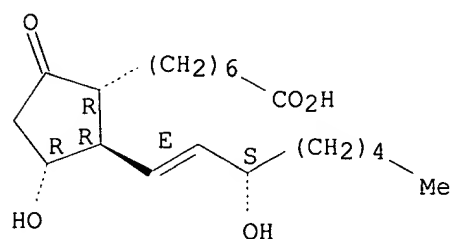
Absolute stereochemistry.  
Double bond geometry as shown.



RN 745-65-3 HCAPLUS

CN Prost-13-en-1-oic acid, 11,15-dihydroxy-9-oxo-, (11 $\alpha$ ,13E,15S)- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



RN 7681-49-4 HCAPLUS

CN Sodium fluoride (NaF) (9CI) (CA INDEX NAME)

F<sup>-</sup> Na

RN 9002-64-6 HCAPLUS

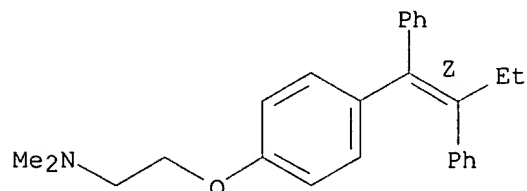
CN Parathormone (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

RN 10540-29-1 HCAPLUS

CN Ethanamine, 2-[4-[(1Z)-1,2-diphenyl-1-butenyl]phenoxy]-N,N-dimethyl- (9CI)  
(CA INDEX NAME)

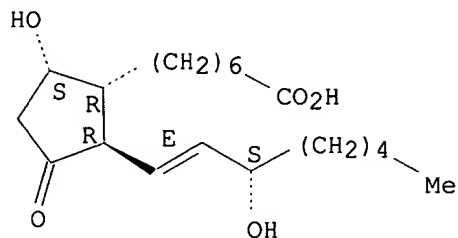
Double bond geometry as shown.



RN 17968-82-0 HCAPLUS

CN Prost-13-en-1-oic acid, 9,15-dihydroxy-11-oxo-, (9 $\alpha$ ,13E,15S)- (9CI)  
(CA INDEX NAME)

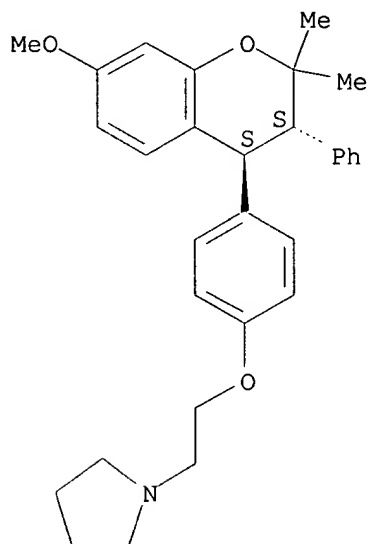
Absolute stereochemistry.  
Double bond geometry as shown.



RN 31477-60-8 HCAPLUS

CN Pyrrolidine, 1-[2-[4-[(3R,4R)-3,4-dihydro-7-methoxy-2,2-dimethyl-3-phenyl-2H-1-benzopyran-4-yl]phenoxy]ethyl]-, rel- (9CI) (CA INDEX NAME)

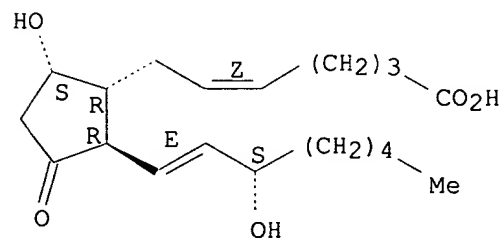
Relative stereochemistry.



RN 41598-07-6 HCAPLUS

CN Prosta-5,13-dien-1-oic acid, 9,15-dihydroxy-11-oxo-, (5Z,9α,13E,15S)- (9CI) (CA INDEX NAME)

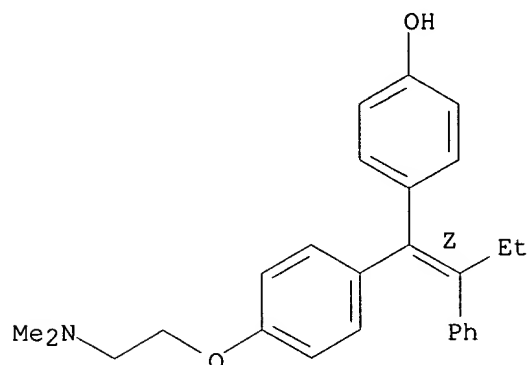
Absolute stereochemistry.  
Double bond geometry as shown.



RN 68047-06-3 HCAPLUS

CN Phenol, 4-[(1Z)-1-[4-[2-(dimethylamino)ethoxy]phenyl]-2-phenyl-1-butenyl]-  
(9CI) (CA INDEX NAME)

Double bond geometry as shown.

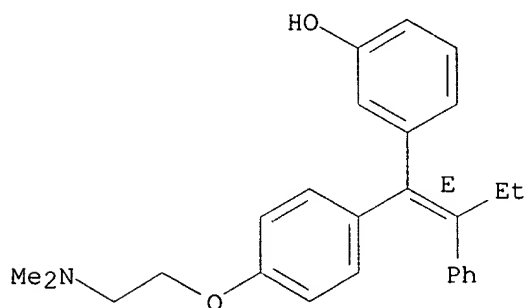


④ 4-hydroxytamoxifen

RN 82413-20-5 HCAPLUS

CN Phenol, 3-[(1E)-1-[4-[2-(dimethylamino)ethoxy]phenyl]-2-phenyl-1-butenyl]-  
(9CI) (CA INDEX NAME)

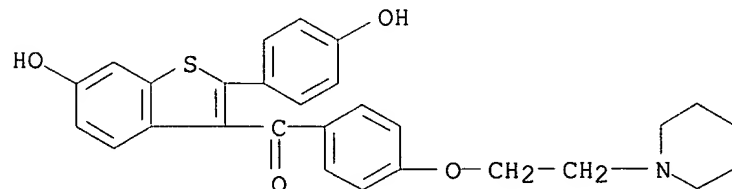
Double bond geometry as shown.



① Droloxifene

RN 84449-90-1 HCAPLUS

CN Methanone, [6-hydroxy-2-(4-hydroxyphenyl)benzo[b]thien-3-yl][4-[2-(1-piperidinyl)ethoxy]phenyl]- (9CI) (CA INDEX NAME)

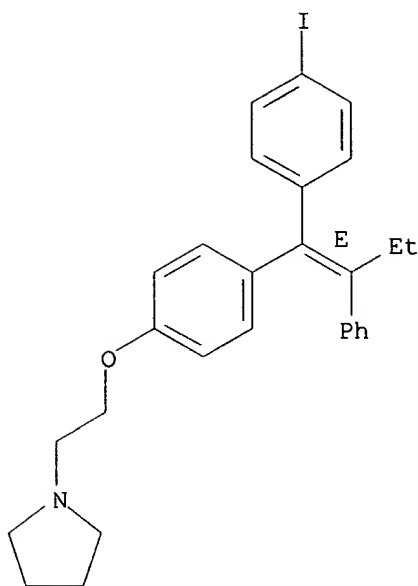


RN 116057-75-1 HCAPLUS

CN Pyrrolidine, 1-[2-[4-[(1E)-1-(4-iodophenyl)-2-phenyl-1-butenyl]phenoxy]ethyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

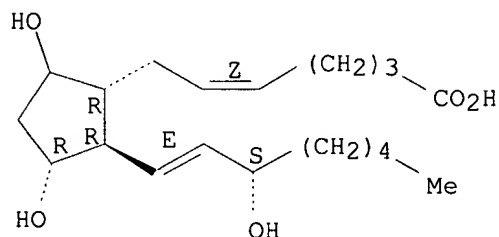




RN 123123-44-4 HCAPLUS

CN Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-, (5Z,11 $\alpha$ ,13E,15S)-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



RN 159752-10-0 HCAPLUS

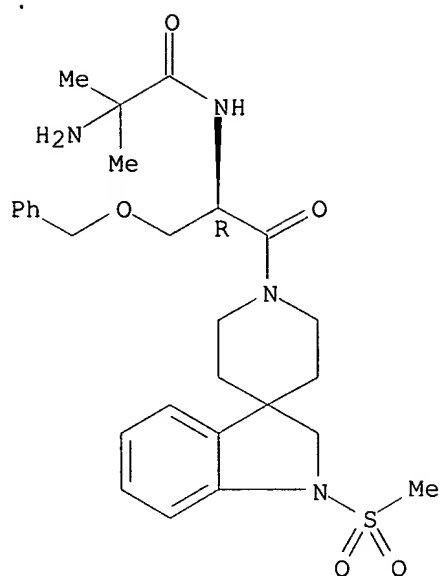
CN Propanamide, 2-amino-N-[(1R)-2-[1,2-dihydro-1-(methylsulfonyl)spiro[3H-indole-3,4'-piperidin]-1'-yl]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]-2-methyl-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 159634-47-6

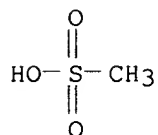
CMF C27 H36 N4 O5 S

Absolute stereochemistry.



CM 2

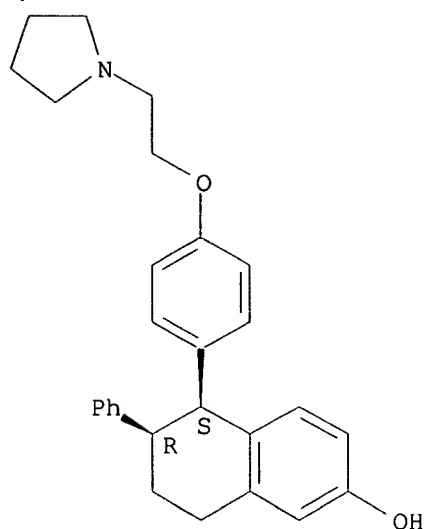
CRN 75-75-2  
CMF C H4 O3 S



RN 180915-78-0 HCAPLUS  
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

⑥

Relative stereochemistry.

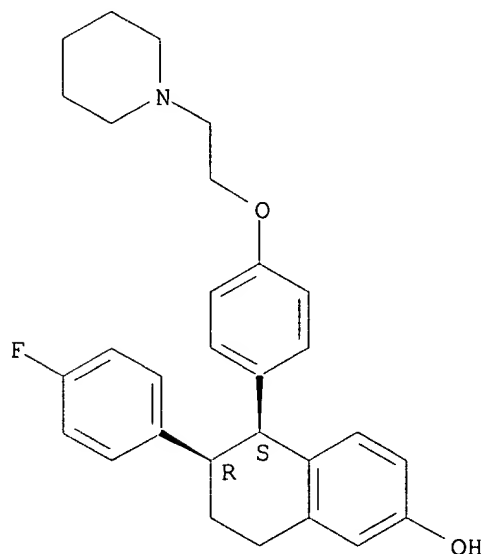


RN 180915-84-8 HCAPLUS

CN 2-Naphthalenol, 6-(4-fluorophenyl)-5,6,7,8-tetrahydro-5-[4-[2-(1-piperidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

(5)

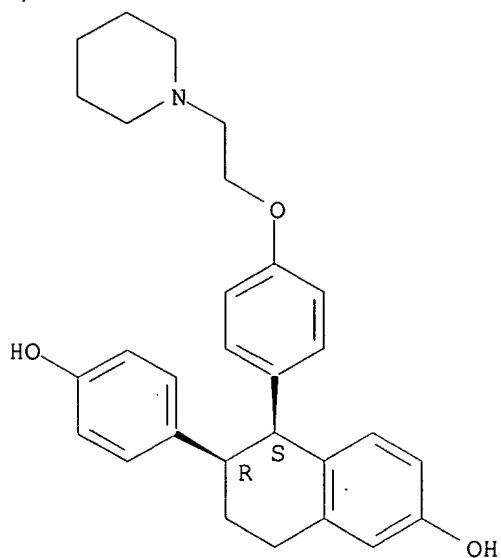


RN 180915-86-0 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-(4-hydroxyphenyl)-5-[4-[2-(1-piperidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

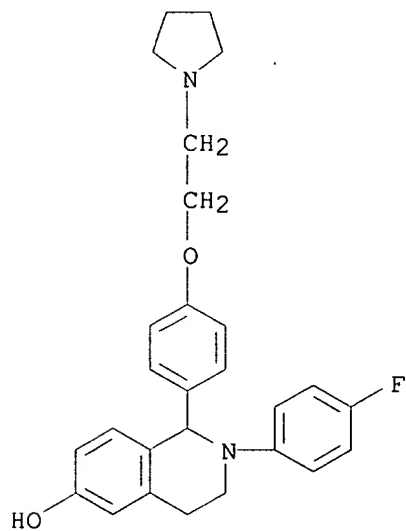
Relative stereochemistry.

(10)



(10)

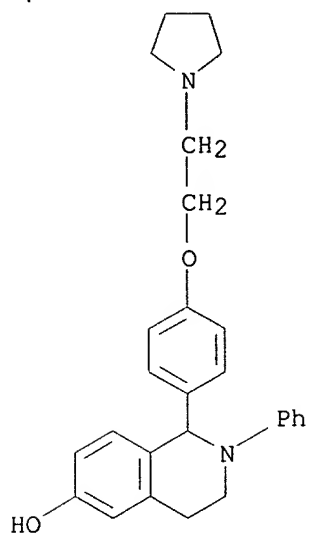
RN 180916-14-7 HCAPLUS  
 CN 6-Isoquinolinol, 2-(4-fluorophenyl)-1,2,3,4-tetrahydro-1-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]- (9CI) (CA INDEX NAME)



(9)

RN 180916-15-8 HCAPLUS  
 CN 6-Isoquinolinol, 1,2,3,4-tetrahydro-2-phenyl-1-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]- (9CI) (CA INDEX NAME)

(11)

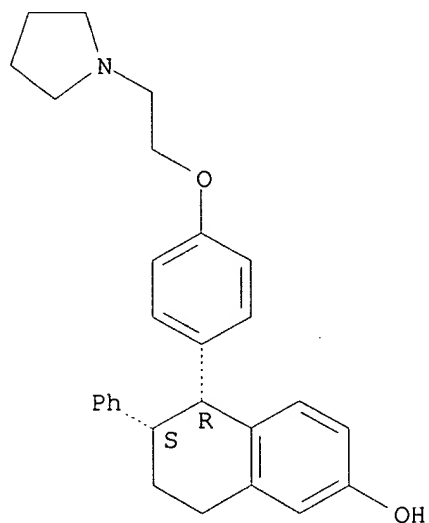


(11)

RN 180916-16-9 HCAPLUS  
 CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

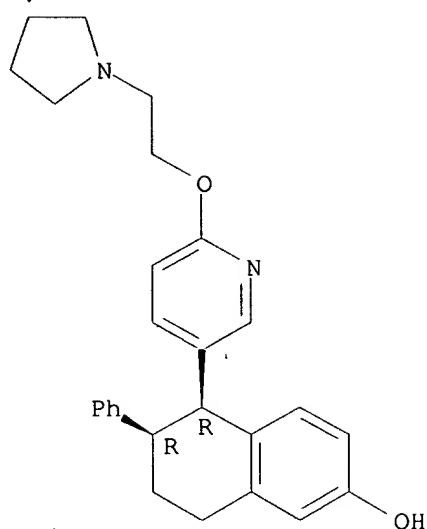
(7)



RN 193274-89-4 HCAPLUS  
 CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[6-[2-(1-pyrrolidinyl)ethoxy]-3-pyridinyl]-, (5R,6R)-rel- (9CI) (CA INDEX NAME)

(8)

Relative stereochemistry.



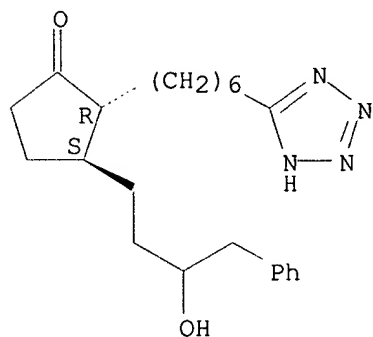
(8)

RN 195962-24-4 HCAPLUS

CN Cyclopentanone, 3-(3-hydroxy-4-phenylbutyl)-2-[6-(1H-tetrazol-5-yl)hexyl]-, (2R,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

(12)



L15 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1995:730370 HCAPLUS

DOCUMENT NUMBER: 123:160785

TITLE: **Droloxifene** prevents ovariectomy-induced **bone loss** in tibiae and femora of aged female rats: a dual-energy x-ray absorptiometric and histomorphometric studyAUTHOR(S): Chen, Hong Ka; **Ke, Hua Zhu**; Jee, Webster S. S.; Ma, Yan Fei; Pirie, Christine M.; Simmons, Hollis A.; **Thompson, David D.**

CORPORATE SOURCE: Division of Radiobiology, Univ. of Utah Sch. of Medicine, Salt Lake City, UT, USA

SOURCE: Journal of Bone and Mineral Research (1995), 10(8), 1256-62

CODEN: JBMREJ; ISSN: 0884-0431

PUBLISHER: Liebert

DOCUMENT TYPE: Journal

## LANGUAGE:

English

AB Our previous studies indicated that **droloxifene** (DRO), a tissue-specific estrogen antagonist/agonist, prevented **bone loss** without causing uterine hypertrophy in growing ovariectomized (OVX) rats. Using dual-energy x-ray absorptiometry (DXA) and bone histomorphometry, the current study compared the efficacy of DRO to  $17\beta$ -estradiol (E2) in preventing OVX-induced **bone loss** in tibiae and femora of 19-mo-old rats to determine whether DRO had similar skeletal effects as E2 in aged female rats. Sprague-Dawley female rats were OVX or sham-operated (sham) at 19 mo of age. The sham-operated rats were treated with vehicle (oral), while the OVX rats were treated with vehicle (oral), E2 at 30  $\mu\text{g/kg/day}$  (s.c.), or DRO at 2.5, 5, or 10  $\text{mg/kg/day}$  (oral) for 8 wk. Bone mineral density (BMD) of whole femora (WF), distal femoral metaphyses (DFM), femoral shafts (FS), and proximal femora (PF) was determined using DXA. Static and dynamic cancellous bone histomorphometric analyses were performed in double-labeled undecalcified longitudinal sections from proximal tibial metaphyses. Ovariectomy for 8 wk significantly reduced the BMD of WF, DFM, FS, and PF (from -6 to -15%). Treatment with E2 completely prevented the decreases in BMD of WF and DFM and had no significant effects in BMD of FS and PF in aged OVX rats. The decrease in BMD of DFM induced by OVX was prevented by treatment with DRO at all dose levels. In addition, DRO at 10  $\text{mg/kg/day}$  prevented OVX-induced decreases in BMD of WF, FS, and PF. Furthermore, proximal tibial cancellous bone histomorphometric results showed that OVX significantly decreased the trabecular bone volume by 34% and increased the activation frequency by 104% while it nonsignificantly increased other indexes including percent eroded perimeter, mineral apposition rate, and bone formation rate per bone volume compared with sham-operated controls. Treatment with E2 or DRO at all dose levels completely prevented the OVX-induced decreases in trabecular bone volume and increases in bone turnover, indicating that DRO is an estrogen agonist in bone in aged OVX rats. Together with the previous findings that DRO inhibited body weight gain, reduced total serum cholesterol, and had no effect on uterine weight, we conclude that DRO is as efficacious as E2 in preventing OVX-induced **bone loss** and inhibiting bone turnover but without estrogenic uterine effects in aged OVX rats. These data suggest that DRO may be superior to E2 for the treatment of postmenopausal and senile **osteoporosis**.

CC 1-12 (Pharmacology)

Section cross-reference(s): 2

ST **droloxifene** bone ovariectomy **osteoporosis**

IT Bone

**Osteoporosis**

## Ovariectomy

(**droloxifene** prevention of ovariectomy-induced **bone loss** in relation to **osteoporosis** treatment)

IT 82413-20-5, **Droloxifene**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(**droloxifene** prevention of ovariectomy-induced **bone loss** in relation to **osteoporosis** treatment)

IT 82413-20-5, **Droloxifene**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

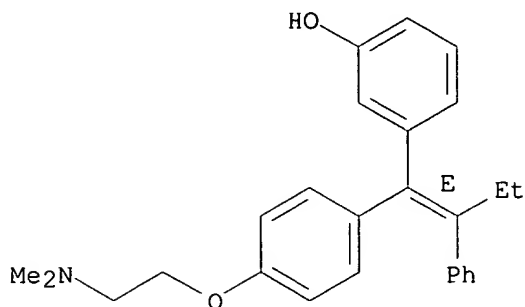
(**droloxifene** prevention of ovariectomy-induced **bone loss** in relation to **osteoporosis** treatment)

RN 82413-20-5 HCAPLUS

CN Phenol, 3-[(1E)-1-[4-[2-(dimethylamino)ethoxy]phenyl]-2-phenyl-1-butenyl]-

(9CI) (CA INDEX NAME)

Double bond geometry as shown.



L15 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1995:575349 HCAPLUS

DOCUMENT NUMBER: 122:306275

TITLE: **Droloxifene**, a new estrogen antagonist/agonist, prevents bone loss in ovariectomized ratsAUTHOR(S): **Ke, Hua Zhu**; Simmons, Hollis A.; Pirie, Christine M.; Crawford, D. Todd; **Thompson, David D.**

CORPORATE SOURCE: Dep. Cardiovascular Metabolic Siseases, Central Res. Div., Groton, CT, 06340, USA

SOURCE: Endocrinology (1995), 136(6), 2435-41  
CODEN: ENDOAO; ISSN: 0013-7227

PUBLISHER: Endocrine Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The purpose of this study was to determine the effects of **droloxifene** (DRO), a new estrogen antagonist/agonist, on bone turnover, bone mass, total serum cholesterol, and uterine weight in rats made estrogen deficient by ovariectomy. Sprague-Dawley female rats were ovariectomized (OVX) or sham operated (sham) at 5 mo of age and treated with 17 $\beta$ -estradiol (E2) at 30  $\mu$ g/kg, s.c., daily or with DRO at 5, 10, or 20 mg/kg·day, orally, for 4 wk. At the time of death, body weight gain, uterine weight, and total serum cholesterol were measured. Bone area, bone mineral content (BMC), and bone mineral d. (BMD) of whole femora, distal femoral metaphases, femoral shaft, and proximal femora were determined ex vivo using dual energy x-ray absorptiometry. Static and dynamic cancellous bone histomorphometric anal. of proximal tibial metaphyses was performed in double **fluorescent** labeled, undecalcified, 4- and 10- $\mu$ m longitudinal sections. Body weight gain in E2-treated OVX rats was significantly reduced compared to that in OVX controls, but was not different from that in sham controls. Body weight gain in DRO-treated OVX rats was decreased significantly compared to that in both sham and OVX controls. In OVX rats, uterine weight was completely preserved by treatment with E2. Uterine weight in DRO-treated OVX rats was slightly, but significantly, increased from the vehicle-treated control value, and was significantly lower than that in sham controls and E2-treated OVX rats. Treatment with s.c. injection of E2 in OVX rats had no effect on total serum cholesterol, whereas OVX rats orally treated with DRO at 5-20 mg/kg·day decreased total serum cholesterol by 33-46% compared to levels in sham and OVX controls. Compared to sham controls, OVX decreased BMC and BMD of distal femoral metaphyses, increased BMD of the femoral



shaft, and had no effect on BMC and BMD of whole femora and proximal femora. Treatment with either E2 or DRO prevented these changes induced by OVX. Proximal tibial metaphyseal trabecular bone volume and trabecular number were increased, and trabecular separation, percent osteoclast perimeter, osteoclast number, percent mineralizing perimeter, mineral apposition rate, bone formation rate, and bone turnover rate were decreased in 5, 10, or 20 mg/kg·day DRO-treated OVX rats compared to OVX controls. These cancellous bone histomorphometric indexes in DRO-treated OVX rats did not differ from those in E2-treated OVX rats or sham controls, suggesting that DRO completely prevented the increases in bone turnover and the decrease in bone mass induced by OVX in rats. The results demonstrate that DRO prevented increased bone turnover and **bone loss**, reduced total serum cholesterol, and caused minimal uterine hypertrophy in 5-mo-old OVX rats. These data suggest that DRO is an estrogen agonist on bone and may be an effective alternative to estrogen for the prevention of postmenopausal **osteoporosis**.

CC 1-10 (Pharmacology)

ST **droloxifene** bone metab

IT Body weight

Bone

Uterus

(**droloxifene**, a new estrogen antagonist/agonist, prevents

**bone loss** in ovariectomized rats)

IT **Osteoporosis**

(postmenopausal, **droloxifene**, a new estrogen antagonist/agonist, prevents **bone loss** in ovariectomized rats)

IT 50-28-2, 17 $\beta$ -Estradiol, biological studies

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(**droloxifene**, a new estrogen antagonist/agonist, prevents **bone loss** in ovariectomized rats)

IT 82413-20-5, **Droloxifene**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(**droloxifene**, a new estrogen antagonist/agonist, prevents **bone loss** in ovariectomized rats)

IT 57-88-5, Cholesterol, biological studies

RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)

(**droloxifene**, a new estrogen antagonist/agonist, prevents **bone loss** in ovariectomized rats)

IT 50-28-2, 17 $\beta$ -Estradiol, biological studies

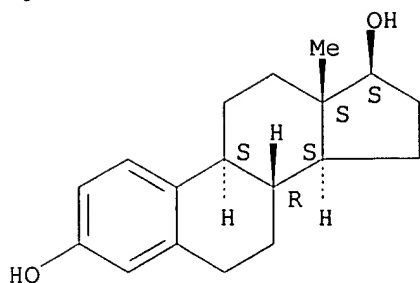
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(**droloxifene**, a new estrogen antagonist/agonist, prevents **bone loss** in ovariectomized rats)

RN 50-28-2 HCAPLUS

CN Estra-1,3,5(10)-triene-3,17-diol (17 $\beta$ )- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 82413-20-5, **Droloxifene**

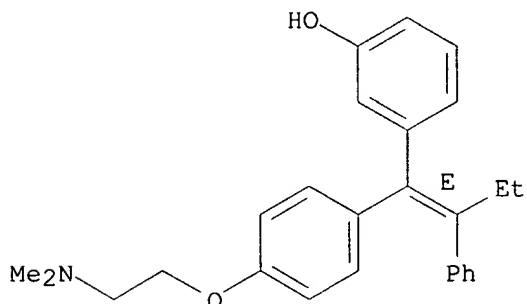
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(**droloxifene**, a new estrogen antagonist/agonist, prevents **bone loss** in ovariectomized rats)

RN 82413-20-5 HCAPLUS

CN Phenol, 3-[(1E)-1-[4-[2-(dimethylamino)ethoxy]phenyl]-2-phenyl-1-butenyl]-(9CI) (CA INDEX NAME)

Double bond geometry as shown.



IT 57-88-5, Cholesterol, biological studies

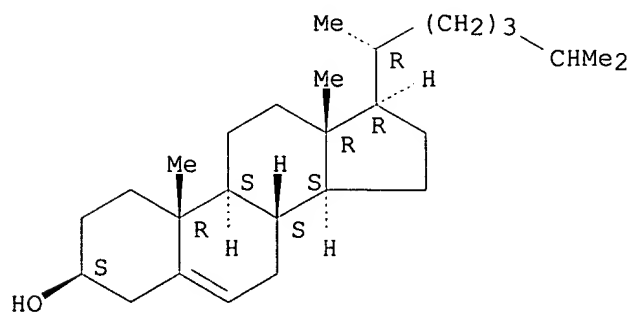
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)

(**droloxifene**, a new estrogen antagonist/agonist, prevents **bone loss** in ovariectomized rats)

RN 57-88-5 HCAPLUS

CN Cholest-5-en-3-ol (3β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> d his ful

(FILE 'HOME' ENTERED AT 11:17:03 ON 14 OCT 2005)

FILE 'HCAPLUS' ENTERED AT 11:17:14 ON 14 OCT 2005

E KE HUA ZHU/AU  
L1 38 SEA ABB=ON ("KE HUA Z"/AU OR "KE HUA ZHU"/AU)  
E THOMPSON DAVID D/AU  
L2 97 SEA ABB=ON ("THOMPSON DAVID D"/AU OR "THOMPSON DAVID DUANE"/AU  
)  
L3 20 SEA ABB=ON L1 AND L2  
L4 17 SEA ABB=ON L3 AND ?OSTEOPOR?  
L5 0 SEA ABB=ON L4 AND ?PAGET?  
L6 12 SEA ABB=ON L4 AND ?BONE?(W)?LOSS?  
L7 3 SEA ABB=ON L6 AND (DROLOXIFENE OR RALOXIFENE OR TAMOXIFEN)  
L8 ANALYZE L7 1-3 CT : 8 TERMS  
SELECT RN L7 1-3

FILE 'REGISTRY' ENTERED AT 11:22:17 ON 14 OCT 2005

L9 14 SEA ABB=ON (50-28-2/BI OR 82413-20-5/BI OR 180915-78-0/BI OR  
180915-79-1/BI OR 180915-93-9/BI OR 180915-96-2/BI OR 180916-16  
-9/BI OR 1845-11-0/BI OR 190791-29-8/BI OR 211797-30-7/BI OR  
4796-75-2/BI OR 57-88-5/BI OR 76313-97-8/BI OR 84449-90-1/BI)

FILE 'HCAPLUS' ENTERED AT 11:22:25 ON 14 OCT 2005

L10 3 SEA ABB=ON L7 AND L9  
D IBIB ABS IND HITSTR L10 1-3  
L11 17 SEA ABB=ON L4 OR L6  
DELETE SELECT  
SELECT RN L11 1-17  
L12 3 SEA ABB=ON L11 AND ?FLUOR?  
L13 5 SEA ABB=ON L10 OR L12  
DELETE SELECT  
SELECT RN L13 1-5

FILE 'REGISTRY' ENTERED AT 11:30:02 ON 14 OCT 2005

L14 36 SEA ABB=ON (180916-16-9/BI OR 82413-20-5/BI OR 180915-78-0/BI  
OR 190791-29-8/BI OR 50-28-2/BI OR 84449-90-1/BI OR 9002-72-6/B  
I OR 10540-29-1/BI OR 116057-75-1/BI OR 123123-44-4/BI OR  
159752-10-0/BI OR 17968-82-0/BI OR 180915-79-1/BI OR 180915-84-  
8/BI OR 180915-86-0/BI OR 180915-93-9/BI OR 180915-96-2/BI OR  
180916-14-7/BI OR 180916-15-8/BI OR 1845-11-0/BI OR 193272-70-7  
/BI OR 193274-89-4/BI OR 195962-24-4/BI OR 211797-30-7/BI OR  
218163-71-4/BI OR 31477-60-8/BI OR 363-24-6/BI OR 41598-07-6/BI  
OR 4796-75-2/BI OR 551-11-1/BI OR 57-88-5/BI OR 68047-06-3/BI  
OR 745-65-3/BI OR 76313-97-8/BI OR 7681-49-4/BI OR 9002-64-6/BI  
)

FILE 'HCAPLUS' ENTERED AT 11:30:11 ON 14 OCT 2005

L15 5 SEA ABB=ON L13 AND L14

FILE 'REGISTRY' ENTERED AT 11:32:49 ON 14 OCT 2005

L16 3 SEA ABB=ON (DROLOXIFENE OR RALOXIFENE OR TAMOXIFEN OR  
4-HYDROXY-TAMOXIFEN)/CN  
E TAMOXIFEN, 4-HYDROXY/CN  
E TAMOXIFEN/CN

FILE 'REGISTRY' ENTERED AT 12:07:47 ON 14 OCT 2005

L17 676 SEA ABB=ON C26H29NO2/MF  
L18 312 SEA ABB=ON L17 AND NRS=3 AND NR=3 AND 46.150.18/RID

L19 STRUCTURE  
L20 19 SEA SSS SAM L19  
L21 STRUCTURE  
L22 8 SEA SSS SAM L21  
E 4-HYDROXY TAMOXIFEN/CN  
E 4-HYDROXY-TAMOXIFEN/CN

FILE 'HCAPLUS' ENTERED AT 12:15:50 ON 14 OCT 2005

L23 198 SEA ABB=ON 4-HYDROXY TAMOXIFEN  
L24 14 SEA ABB=ON L23 AND ?BONE?

FILE 'REGISTRY' ENTERED AT 12:17:03 ON 14 OCT 2005

L25 1 SEA ABB=ON 68047-06-3/RN  
L26 4 SEA ABB=ON (82413-20-5 OR 84449-90-1 OR 10540-29-1 OR  
68047-06-3)/RN  
L27 7 SEA ABB=ON (180915-84-8 OR 180915-78-0 OR 180916-16-9 OR  
193274-89-4 OR 180916-14-7 OR 180915-86-0 OR 180916-15-8)/RN  
L28 11 SEA ABB=ON L26 OR L27  
L29 4 SEA ABB=ON (PGD1 OR PGD2 OR PGE2 OR PGE1 OR PGF2 OR PGF2A)/CN  
E PGF/CN  
L30 1 SEA ABB=ON PGF2A/CN  
L31 5 SEA ABB=ON L29 OR L30  
L32 6 SEA ABB=ON L31 OR 195962-24-4/RN

FILE 'HCAPLUS' ENTERED AT 12:54:44 ON 14 OCT 2005

L33 10983 SEA ABB=ON L28 OR ?DROLOXIFENE? OR ?RALOXIFENE? OR ?TAMOXIFEN?  
L34 173 SEA ABB=ON L33 AND (L32 OR PGD1 OR PGD2 OR PGE2 OR PGE1 OR  
PGF2 OR PGF2A OR PGF2A)  
L35 6 SEA ABB=ON L34 AND (?BONE?(W) (?LOSS? OR ?LOSE? OR ?RESORP) OR  
?OSTEOPOROS? OR ?PAGET?)  
L36 0 SEA ABB=ON L35 AND (PRD<19960228 OR PD<19960228)

FILE 'MEDLINE, BIOSIS, CANCERLIT, EMBASE, JAPIO, JICST-EPLNS' ENTERED AT  
12:58:15 ON 14 OCT 2005

L37 21 SEA ABB=ON L35  
L38 16 DUP REMOV L37 (5 DUPLICATES REMOVED)

FILE 'USPATFULL' ENTERED AT 12:59:12 ON 14 OCT 2005

L39 1 SEA ABB=ON L35 AND (PRD<19960228 OR PD<19960228)

FILE HOME

FILE HCAPLUS

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FILE COVERS 1907 - 14 Oct 2005 VOL 143 ISS 17  
FILE LAST UPDATED: 13 Oct 2005 (20051013/ED)

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identified from  
inventor search -  
see markings  
in that search*

*This one didn't  
show up in Registry*

*Cite's before your  
specified date*

*16 cite's from above db's*

*1 cit from  
USPatfull*

This file contains CAS Registry Numbers for easy and accurate substance identification.

#### FILE REGISTRY

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 12 OCT 2005 HIGHEST RN 865114-63-2  
DICTIONARY FILE UPDATES: 12 OCT 2005 HIGHEST RN 865114-63-2

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

\*\*\*\*\*  
\*  
\* The CA roles and document type information have been removed from \*  
\* the IDE default display format and the ED field has been added, \*  
\* effective March 20, 2005. A new display format, IDERL, is now \*  
\* available and contains the CA role and document type information. \*  
\*  
\*\*\*\*\*

Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

#### FILE MEDLINE

FILE LAST UPDATED: 13 OCT 2005 (20051013/UP). FILE COVERS 1950 TO DATE.

On December 19, 2004, the 2005 MeSH terms were loaded.

The MEDLINE reload for 2005 is now available. For details enter HELP RLOAD at an arrow prompt (=>). See also:

<http://www.nlm.nih.gov/mesh/>  
[http://www.nlm.nih.gov/pubs/techbull/nd04/nd04\\_mesh.html](http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html)

OLDMEDLINE now back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2005 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

#### FILE BIOSIS

FILE COVERS 1969 TO DATE.

CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 12 October 2005 (20051012/ED)

FILE RELOADED: 19 October 2003.

FILE CANCERLIT

FILE COVERS 1963 TO 15 Nov 2002 (20021115/ED)

On July 28, 2002, CANCERLIT was reloaded. See HELP RLOAD for details.

CANCERLIT thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2002 vocabulary. Enter HELP THESAURUS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE EMBASE

FILE COVERS 1974 TO 13 Oct 2005 (20051013/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE JAPIO

FILE LAST UPDATED: 4 OCT 2005 <20051004/UP>

FILE COVERS APR 1973 TO MAY 26, 2005

<<< GRAPHIC IMAGES AVAILABLE >>>

FILE JICST-EPLUS

FILE COVERS 1985 TO 12 OCT 2005 (20051012/ED)

THE JICST-EPLUS FILE HAS BEEN RELOADED TO REFLECT THE 1999 CONTROLLED TERM (/CT) THESAURUS RELOAD.

FILE USPATFULL

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 13 Oct 2005 (20051013/PD)

FILE LAST UPDATED: 13 Oct 2005 (20051013/ED)

HIGHEST GRANTED PATENT NUMBER: US6954941

HIGHEST APPLICATION PUBLICATION NUMBER: US2005229280

CA INDEXING IS CURRENT THROUGH 13 Oct 2005 (20051013/UPCA)

ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 13 Oct 2005 (20051013/PD)

REVISED CLASS FIELDS (/NCL) LAST RELOADED: Aug 2005

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